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THESIS

A HIGH EXPLANATORY POWER MODEL OF FOOT AND MOUTH DISEASE SPREAD IN CENTRAL CALIFORNIA

by

Diwya Alok

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The main takeaways of our analysis of FMD spread are as follows. The two most critical disease parameters are initial condition and local spread. The most critical disease control parameters are market movement and surveillance. Our experimental results indicate that if a typical premise sends an animal to market every 2.2 days instead of every day, we will see a 25% reduction in the mean number of cattle infected. Similarly, if there is less than a three day delay in between suspecting an FMD outbreak and declaring an FMD outbreak at dairy-like facilities, we see a 50% reduction in the number of infected cattle. Control measures cannot be taken in isolation. Our models show significant interaction effects between the most effective control measures—market movement, and surveillance—and other control measures such as tracing, vaccination and depopulation.

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A HIGH EXPLANATORY POWER MODEL OF FOOT AND MOUTH DISEASE SPREAD IN CENTRAL CALIFORNIA

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LIST OF ACRONYMS AND ABBREVIATIONS

APHIS	Animal and Plant Health Inspection Service
ANOVA	Analysis of Variance
ARP	At Risk Premises
BZ	Buffer Zone
CA	Control Area
CalTrans	California Department of Transportation
CCS83	California Coordinate System 83
CDFA	California Department of Food and Agriculture
CP	Contact Premises
CSV	Comma Separated Value
CVO	Chief Veterinary Officer of the United States
DEFRA	Department for Environment, Food and Rural Affairs
DOE	Design of Experiment
FADDL	Federal Foreign Animal Disease Diagnostic Laboratory
FADPReP	Foreign Animal Disease Preparedness and Response Plan
FIPS	Federal Information Processing Standard
FMD	Foot and Mouth Disease
FMDV	Foot and Mouth Disease Virus
FP	Free Premises
GAO	U.S. General Accounting Office
IP	Infected Premises
ISP	InterSpread Plus
IZ	Infected Zone
Km	Kilometer
Lat	Latitude
LLNL	Lawrence Livermore National Laboratory
Long	Longitude
M	Meter

MOE	Measure(s) of Effectiveness
MP	Monitored Premises
NAHEMS	National Animal Health Emergency Management System
NASS	National Agricultural Statistics Service
NCIE	National Center for Import and Export
NIMS	National Incident Management System
NOLH	Nearly Orthogonal Latin hypercube
NRF	National Response Framework
NSTC	National Science and Technology Council
NVSL	National Veterinary Services Laboratories
OIE	World Organization for Animal Health
SAHO	State Animal Health Official
SEED	Simulation Experiments and Efficient Design
SITC	Smuggling Interdiction and Trade Compliance
SP	Suspect Premises
SS	Sum of Squares
Std Dev	Standard Deviation
SZ	Surveillance Zone
U.K.	United Kingdom
U.S.	United States
USDA	U.S. Department of Agriculture
VP	Vaccinated Premises
VZ	Vaccination Zone

EXECUTIVE SUMMARY

Foot and mouth disease (FMD) has a devastating impact on a country's economy. The FMD containment process demands considerable efforts in vaccination, monitoring, trade restrictions, quarantines, and, historically, the elimination of millions of animals. Although, no incidence of FMD has been reported in the United States (U.S.) since 1929, there is a chance of its introduction as the disease is prevalent in two-thirds of the world. The United Kingdom (U.K.) had been free of FMD for more than 30 years before a major epidemic occurred in 2001. The epidemic resulted in the slaughter of approximately 7 million animals and had an estimated economic impact of $11.9–$18.4 billion by direct and indirect losses. A study conducted by Carpenter, O'Brien, Hagerman and McCarl in 2011, estimate the economic impact of a Foot and mouth disease (FMD) epidemic in the U.S. to be $2.3–$69.0 billion.

The U.S. Department of Agriculture is the lead agency for coordinating the response plan during an FMD outbreak. The national response plan is detailed in the Red Book (2012). The planning for the containment of the disease involves prior investments in control options, which determine the availability of response measures.

We simulate an outbreak of FMD across central California using the state of the art disease modeling Interspread Plus simulation package. We explore the epidemic's response to varying disease and control parameters using an experimental design. We carry out 50 replications of 2,048 design points to produce 102,400 epidemic simulation runs. We execute the simulation runs on a cluster of computers. Using the data from the simulations, we identify 16 critical disease and control parameters that have the greatest effect on the spread of FMD. A statistical model based on these 16 parameters and their interactions captures approximately 85% of the variability of the simulation model.

The main takeaways of our analysis of FMD spread are as follows:

- *Initial Condition*: The initial condition of the disease plays a significant role in the spread of the disease. We consider four starting scenarios: high animal density region, high premise density region, market, and port of San Francisco. Among the scenarios, the disease spread is almost twice as high when the infection originates in

high animal or high premise dense areas. Detection time is, however, 28% shorter if the initial infection originates in high premise or high animal dense areas.

- *Local Spread*: The local spread parameter captures the proximity-based spread of FMD between premises. Out of all disease and control parameters, epidemic progression has the highest sensitivity to local spread. Interaction and non-linear effects are significant for this parameter. Restricting local spread to less than 4,000 meters results in a 1.42 fold reduction in the mean number of cattle infected; however, the extent to which we can restrict local spread in a real-world scenario is unknown.

- *Market Movement*: Market movement of cattle is a major contributor towards the spread of the disease. Interaction and non-linear effects for market movement are significant for this parameter. Our experimental results indicate that if a typical premise sends an animal to market every 2.2 days instead of every day, we will see a 25% reduction in the mean number of cattle infected.

- *Surveillance*: Surveillance measures at dairy-like facilities are highly significant. We observe high positive interactions between surveillance and other control measures such as tracing and depopulation. Among the control measures, surveillance has the maximum impact towards reducing the spread of the disease. If there is less than a three day delay between suspecting an FMD outbreak and declaring an FMD outbreak at dairy-like facilities, we see a reduction in mean detection time for a novel epidemic of 32%. A delay of less than two days in the same parameter reduces the average number of infected cattle by half.

Control measures cannot be taken in isolation. Our models show significant interaction effects between the most effective control measures—market movement, and surveillance—and other control measures such as tracing, vaccination and depopulation. In addition, our model suggests that restricting local spread and controlling direct, indirect and market movements can be decisive towards controlling the spread of the disease in California. Furthermore, surveillance measures and movement control in adjoining zones, in addition to the primary outbreak zone, may help in reducing disease spread.

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I. INTRODUCTION

A. PURPOSE

Foot and mouth disease (FMD), also called hoof-and-mouth disease, is an infectious and sometimes fatal viral disease that affects cloven-hoofed animals. Foot and mouth disease virus (FMDV) is highly contagious and causes significant reduction in the productivity of many species, with substantial mortality in the young (Steven, 2010). Outbreaks in FMD free regions pose immediate challenges for policy makers. As seen in Figure 1, FMD exists in almost two thirds of the world. There is always a chance that FMD can either accidentally or through agricultural terrorism be introduced into the United States (U.S.).

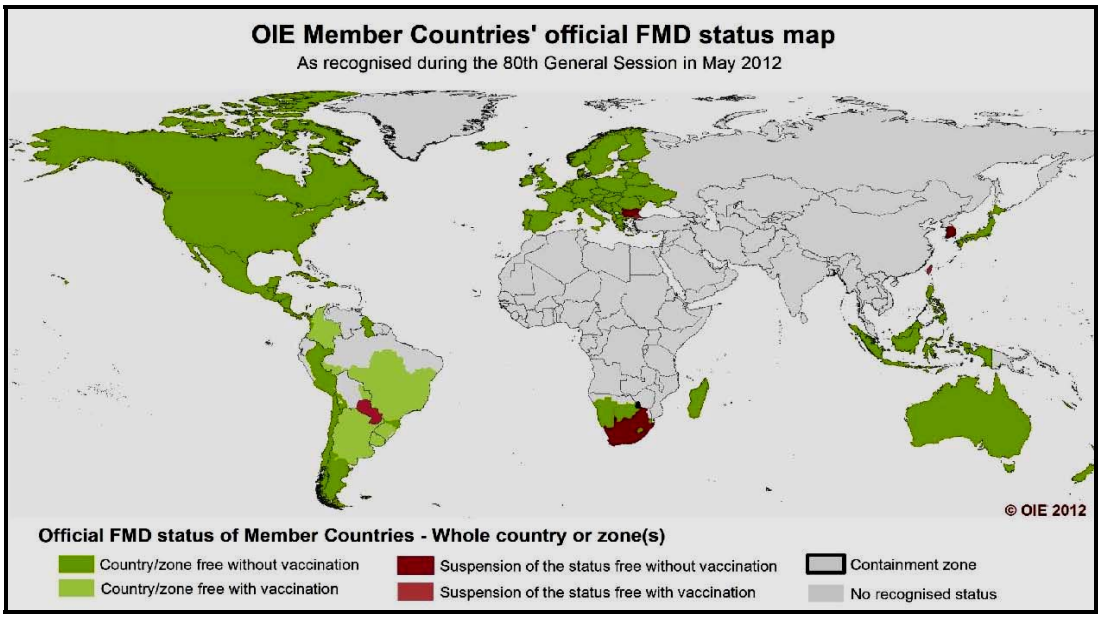

Figure 1. FMD status map issued by Organization of International des Epizooties (OIE)—an animal World Health Organization. OIE recognized the FMD Status of nations in the 80th General Session in May 2012. The FMD status map shows only one third of the world (highlighted in dark and light green) to be free from FMD with or without vaccination.

Livestock animals are highly susceptible to FMD virus (Steven, 2010). If an outbreak occurred in the U.S., this disease could spread rapidly to all sections of the

country through direct contact between susceptible and infected livestock or through fomites, such as footwear, clothing, and equipment. Under favorable conditions, air borne spread through aerosol could also be a carrier of the disease.

FMDV is an extremely robust virus that can persist for weeks or months given favorable environmental conditions. The FMD containment process demands considerable efforts in vaccination, strict monitoring, trade restrictions and quarantines, and occasionally the elimination of millions of animals. Susceptible animals include cattle, water buffalo, sheep, goats, pigs, antelope, deer, hedgehogs, elephants, llama, alpaca and bison. FMD is only rarely transmitted to humans; however, it does indirectly affect human health through increased incidence of clinical depression and post-traumatic stress (USDA APHIS, The Red Book, 2012).

The loss of revenue for a country due to an FMD outbreak can be extensive. The epidemic of FMD in the United Kingdom (U.K.) in 2001 provides one example. The epidemic spread rapidly and infected more than 2,000 farms throughout Britain. Around seven million sheep and cattle were killed before the authorities could halt the spread. Estimates place the cost of the epidemic at £8 billion ($16 billion) to the agricultural and support industries (Alderson, 2001). Detailed study indicates that the epidemic was probably caused by pigs that had been fed garbage containing remains of infected meat that had been illegally imported to Britain (DEFRA, 2002).

No case of an FMD outbreak has been reported in the U.S. since 1929. However, given the susceptibility of an outbreak, U.S. can suffer extensive financial losses. We undertake simulation of the outbreak using the state of the art disease modeling InterSpread Plus (ISP) software. We use a Nearly Orthogonal Nearly Balanced Design of Experiment to derive meaningful outputs for cost effective control, early detection and eradication of the disease. The experimental design ensures low pairwise correlation amongst any two factor columns so that the first order effect estimates are nearly independent. Based on the output of the simulation runs we evaluate control strategies. We analyze the factors that contribute towards the spread of the disease and identify control measures that can be used to reduce the spread.

B. BACKGROUND

1. History and Global Relevance

The earliest description of what was probably FMD was given by Hieronymi Fracastorii, an Italian physician (1546). He described the disease, which occurred in Northern Italy in 1514, as being unusual and affecting only cattle. The cause of FMD was first shown to be viral in 1897 by Friedrich Loeffler, a German bacteriologist at the University of Greifswald. Since then, detailed studies have been undertaken, as FMD is recognized as a highly contagious disease, capable of infecting nearly 70 species within 20 families of mammals (Knowles, 1990). Amongst the host, cattle are the most susceptible and pigs spread the virus most rapidly. Pigs produce 30 to 100 times as much virus in aerosols as sheep or cattle (WRLFMD, 2011). After World War II, the disease spread throughout the world. As seen in Figure 2, FMD exists in two thirds of the world and is endemic in parts of Africa, Asia, Eastern Europe, Middle East, and South America. North America, Central America, Western Europe, Australia, and New Zealand are free of FMD.

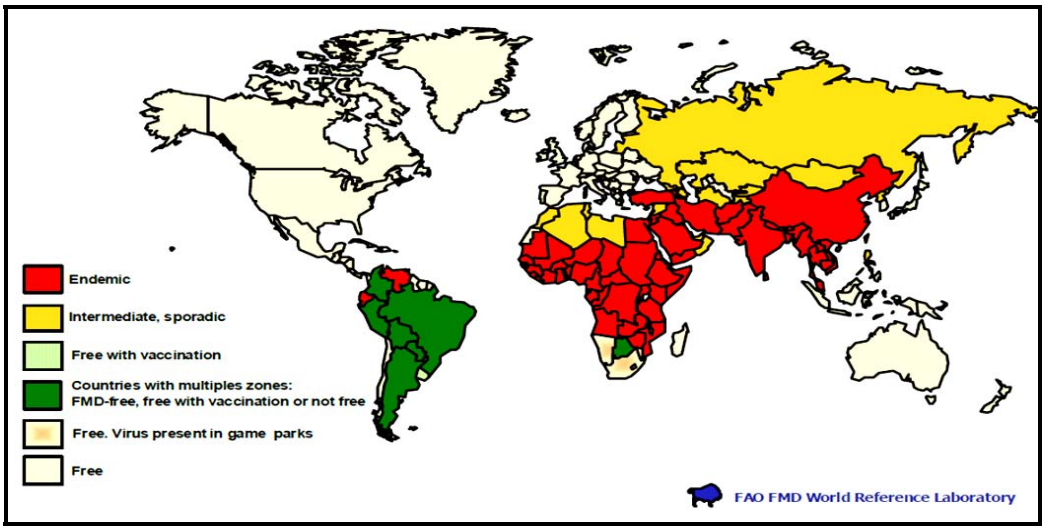

Figure 2. Conjectured Status of FMD Endemic Nations World Map—FAO FMD World Reference Laboratory issued a Conjectured Status of FMD World Map in 2010 indicating the FMD Status of the nations. Countries highlighted in red are still endemic to the disease. The picture shows that FMD exists in almost two thirds of the world.

The FMDV generally does not affect humans. Amongst the seven variations of the species of the virus, serotype O was responsible for the outbreak in Taiwan in 1997, later spreading to Korea and Japan in 2000, and for the outbreak in the U.K. in 2001. Figure 3 shows FMD outbreaks that have occurred in 2011 in countries including Japan, China, Kazakhstan, Botswana, Bulgaria, Nigeria, Zimbabwe, South Africa, South Korea, Namibia, and North Korea. Many of these outbreaks occurred outside endemic infection zones (DEFRA 2011).

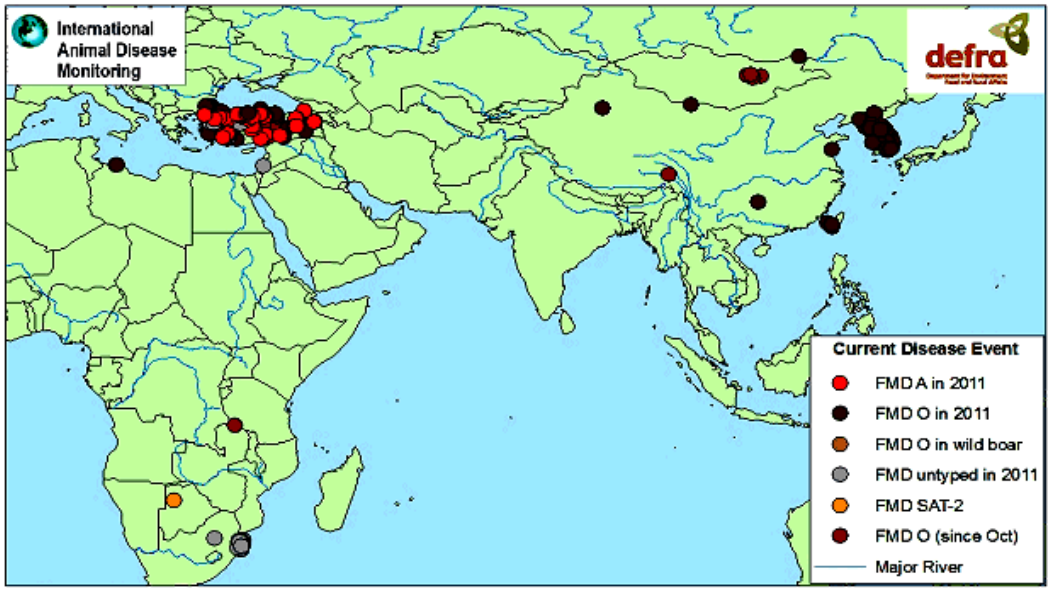

Figure 3. Recent FMD Outbreaks in Africa, Asia and the Middle East in 2011 (From DEFRA 09, released on 14 Apr 2011). The map represents the prevalence of the disease in the contemporary world. We also observe that serotype O was the most common cause for the spread of the disease in Africa and Asia in 2011. In our simulation, we model serotype O to be the cause of the initial infection in the U.S.

Since 1870, the U.S. has had nine FMD outbreaks. Among these, the most economically devastating outbreak occurred in 1914. The FMDV originated in Michigan, but soon entered the stockyards in Chicago. Over 170,000 cattle, sheep and swine were infected across the U.S.. It cost the country $4.5 million to earn a FMD free status. Another FMD outbreak occurred in California in 1924 which resulted in the slaughter of 109,000 farm animals and 22,000 deer. The last FMD outbreak in the U.S. was in Montebello, California in 1929. The virus originated in hogs that had eaten infected meat scraps. Over 3,600 animals were slaughtered. It almost took a month to contain the disease (CSR Report, 2001). Since 1929, U.S. has rigorously maintained FMD free status.

2. Impact of an FMD Outbreak

Economic impacts can be direct and indirect. The direct cost can be subdivided into primary and secondary costs. Direct primary costs are disease management costs and

carcass disposal costs. Consequences of agricultural contamination could affect other sectors of the economy as well. Such losses are termed secondary losses. An example of direct secondary loss is international trade impacts where exports of livestock and livestock products will have impacts reaching into infected regions not infected by FMD. Indirect cost is primarily concerned with the consumer and employment effects and losses to related industries such as the tourism industry.

History has been testimonial to the fact that countries that were FMD free for decades suddenly found themselves plagued with the disease. In 1997, prior to the 2001 U.K. outbreak, Taiwan encountered this epidemic in spite of being FMD free for sixty-seven years. In this case, FMDV was highly virulent in swine but was less effective in other cloven hoofed species. Within six weeks, FMDV infected a total of 6,147 pig farms, hitting the country's swine industry. Taiwanese hog prices dropped 60 percent within a week. The pig industry suffered a loss of $1.6 billion as the pork export market to Japan was almost shut down. Approximately 4 million animals were slaughtered and approximately 65,000 workers lost their jobs (Carpenter, O'Brien, Hagerman and McCarl, 2011). The country lost more than $6 billion as direct and indirect losses to recover from the disease. So devastating was the effect that before the 1997 outbreak, Taiwan was one the worlds leading pork exporters, but today it is a net importer. There are several other examples that imply the devastating consequences of this highly contagious disease. However, we will restrict ourselves to the impact due to an outbreak of FMD in California.

A 2007 FMD simulation model predicts that if an outbreak of FMD originates in California, then national trade losses would exceed $700 million with an overall economic impact of $8.5 billion to $13.5 billion depending on the diagnostic delays (Carpenter, Christiansen, Dickey, Thunes and Hullinger, 2007). International agriculture product markets would be worst hit. Simulation models establish direct correlation between the delay in detecting the presence of the FMDV and delays in implementation of appropriate control and eradication measures. Countries that are FMD free are likely to experience more diagnostic delays as farms and markets will not suspect contamination

until clinical signs show. Several simulation studies have been undertaken to cater for diagnostic delays. We carry out a literature review in section D to understand the previous work undertaken in this field.

3. Causality and Diagnosis

The FMDV is a member of the genus Aphthovirus and belongs to the Picornaviridae family. The USDA APHIS, Veterinary Services defines FMDV as "an etiologic agent of an acute systemic vesicular disease affecting cloven-hoofed animals worldwide." There are seven immunologically distinct serotypes—O, A, C, SAT 1, SAT 2, SAT 3 and Asia 1 with over 65 strains within these serotypes. As seen in Figure 4, FMDV serotypes and strains are specific to geographic regions. Immunity to one serotype does not provide any cross-protection to others (USDA APHIS 2012).

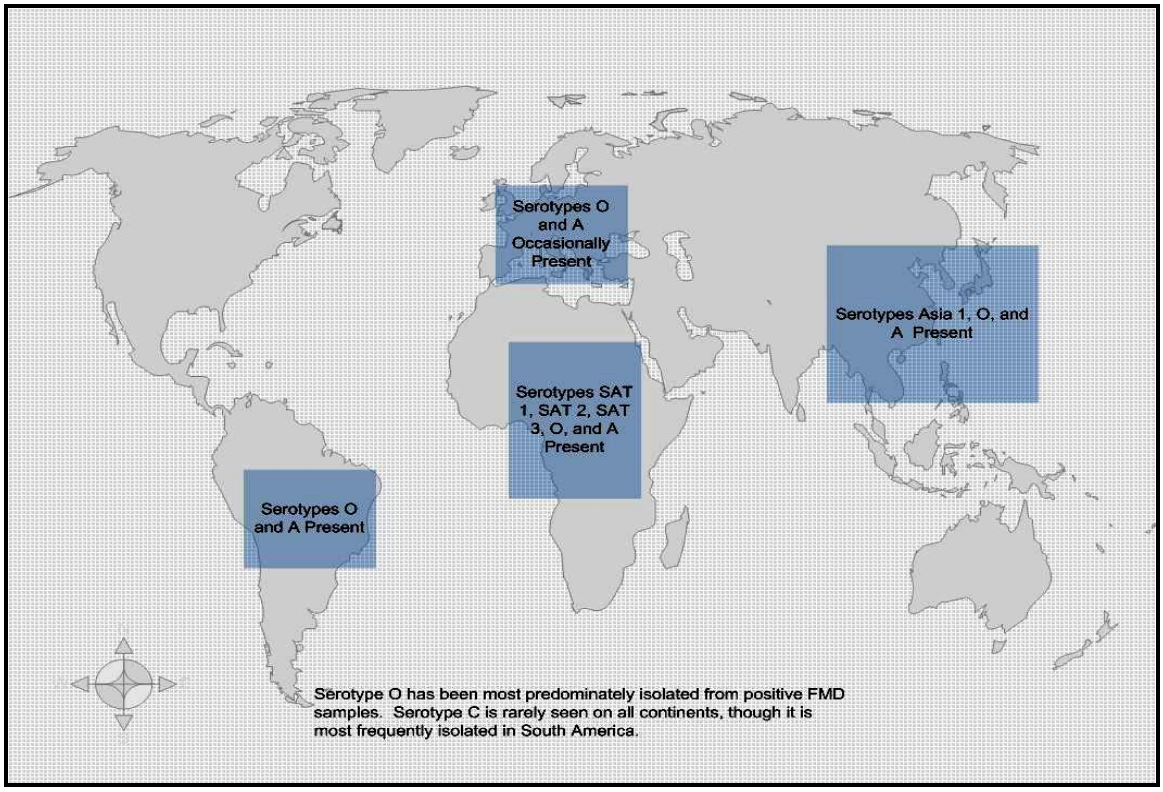

Figure 4. Regional distribution of serotypes of FMD worldwide (From USDA APHIS FMD Response Plan: The Red Book, June 2012). We observe that serotype O is the most common and has been diagnosed in almost all parts of the world followed by serotype A.

The disease is highly contagious as all types of secretions and excretions from infected animals can spread the virus. FMDV can be spread by infected animals up to four days prior to the onset of clinical signs. Vesicle rupture is the most infectious route of virus transmission. FMDV transmissions occur due to direct or indirect contact with infected animals and contaminated fomites. The common routes of contracting the disease include inhalation of the aerosolized virus, ingestion of contaminated feed, and entry of the virus through skin abrasions or mucous membranes (Aftosa, 2007). FMDV can also spread via aerosol transmission under favorable environmental conditions. Pigs, particularly, excrete large amounts of virus through their respiratory tract, which can lead to infectious aerosols that can be inhaled by other animals (typically cattle) in their proximity. FMDV also spreads through windborne transmission. The distance of windborne transmission depends on the atmospheric conditions and the concentration of the virus in the air. FMDV may spread up to 6—90 km over land in favorable conditions such as high relative humidity, steady wind, minimal convection currents, and lack of topographical obstructions (Donaldson, 2002).

FMD is not considered a public health threat, as cases of FMD in humans are very rare. The disease in humans is mild and transient. In humans, FMDV may be carried in the nasal passages for about 24 hours allowing people who have been in close contact with infected animals to potentially serve as a carrier of the virus. However, good personal hygiene and strict biosecurity protocols may totally restrict the transmission. (USDA APHIS, 2012)

Early diagnosis is critical in restricting the spread of FMD. It is therefore expected that all producers, farm owners and veterinarians are familiar with the clinical signs of FMD as they are the ones who are likely to be the initial detectors of the disease. Depending on the intensity of the virus, type of species and the medium of spread, the FMDV incubation period may vary between 2–14 days (WRLFMD, 2011). The incubation period for pigs is two days or more, but in some cases they have been documented to be as short as 18–24 hours. For sheep, the period varies from three to eight days.

The symptoms and severity of the disease vary with the species of animals, the serotype and the strain of FMDV. As seen in Figure 5, vesicles on the feet, in and around the mouth, and on the mammary glands, accompanied with fever, are the general symptoms for FMD. At times, vesicles may occur at the vulva or at pressure points on the legs. Rupture of vesicles cause tremendous pain and discomfort that leads to depression and anorexia. FMDV leads to excessive salivation and lameness amongst the affected animals. In some cases, abortion may occur in pregnant animals. Two to three weeks is the normal recovery time for most adults. Some cases with secondary infections may have a longer recovery time. FMD may lead to temporary or permanent decrease in milk production, chronic lameness and weight loss.

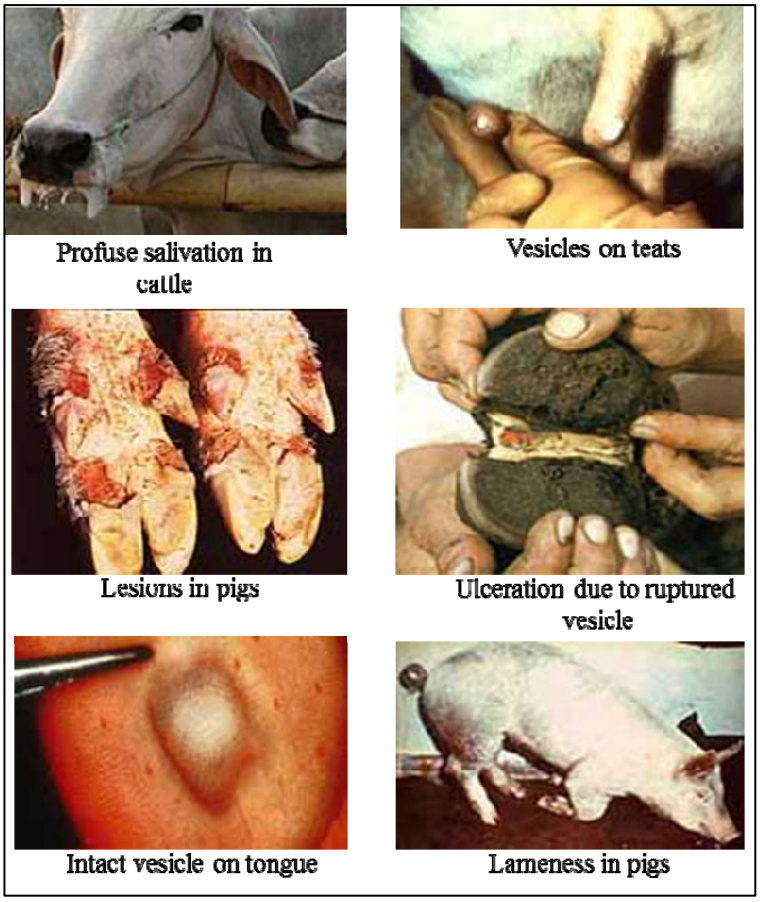

Figure 5. Clinical Signs of FMD. (From FAO, U.N., Issued in public interest for an early identification of the lesions of FMD. Early identification is istrumental in reducing the spread of FMDV

C. CURRENT PREPEREDNESS AND RESPONSE

1. Framework

Successful emergency preparedness and response to FMD is achieved by seamless integration between the National Response Framework (NRF), the National Incident Management System (NIMS), and the National Animal Health and Emergency Management System (NAHEMS). The NRF provides a guideline for the conduct of an emergency response at the national level. NIMS bind departments and agencies at all levels of government with private sector and non-governmental organizations through a seamless proactive approach plan (USDA APHIS, 2012). NAHEMS provides a functional framework for responding to foreign animal disease (FAD) emergencies. Federal response to the detection of a FAD such as FMD is based on the response structure of NIMS as outlined in the NRF.

United States Department of Agriculture (USDA) APHIS has the primary responsibility and authority for animal disease control. It serves as an important link between federal states, tribal, and local partners in FMD eradication and control efforts. In addition, it operates several National Veterinary Services Laboratories (NVSL) like the Foreign Animal Disease Diagnostic Laboratory (FADDL) for the detection of FMDV (USDA APHIS, 2012).

USDA APHIS conducts multiple preparedness exercises that simulate an FMD outbreak. A federal level response effort is simulated across the U.S. These exercises allow various agencies to discuss and practice measures such as movement control, and to evaluate the social and economic impact of a potential outbreak. Multi-state mock exercises increase coordination between the states themselves and between states and the federal government. Following sections of the USDA enforce stringent measures to protect the country from an outbreak of FAD:

- *Smuggling Interdiction and Trade Compliance (SITC).* SITC conducts risk evaluation checks and anti-smuggling drives to prevent unlawful ingress and further distribution of contaminated agricultural

products. It keeps all the domestic markets under surveillance that may have illegal imported animal products.

- *National Center for Import and Export (NCIE)*. NCIE ensures proper medical disease free certification of animals presented at the border and also regulates the import and export of animals and animal products. According to regulations, before export to the U.S., all cattle must be quarantined for 60-days. In addition, all cattle (except those from Canada and Mexico) are kept for a 30-day quarantine at a USDA Animal Import Center. U.S. does not import livestock from countries affected with FMD.

2. Response Goals and Strategies

USDA APHIS (2012) defines:

> The goals of an FMD response are to (1) detect, control, and contain FMD in animals as quickly as possible; (2) eradicate FMD using strategies that seek to stabilize animal agriculture, the food supply, the economy, and protect public health; and (3) provide science- and risk-based approaches and systems to facilitate continuity of business for non-infected animals and non-contaminated animal products.

The primary aims of these three goals are to facilitate earliest resumption of an FMDV free livestock industry in the country through an economically viable response effort that causes lesser disruption and financial losses as compared to the FMD outbreak itself. There are four recognized strategies for the control and eradication of FMD in domestic livestock following an outbreak.

- *Stamping-Out*. Stamping—out involves depopulation of clinically affected and in-contact susceptible animals. This strategy is adopted when it is confirmed that the outbreak is restricted to a jurisdictional area or a region in which the spread of FMDV can be readily contained and further dissemination is unlikely.

- *Stamping-Out Modified with Emergency Vaccination to Slaughter*. This strategy includes depopulation of affected and in-contact susceptible animals and vaccination of at-risk animals. Vaccinated animals will

subsequently be slaughtered. This strategy is adopted when the goal is to restrict the virus replication in high risk susceptible animals. This is achieved through the use of emergency vaccination followed by slaughtering of the vaccinates at pre-determined stages and locations under consultation with the U.S. Chief Veterinarian Officer (CVO) and the State Animal Health Official (SAHO).

- *Stamping-Out modified with emergency vaccination to live*. This strategy includes depopulation of affected and in-contact susceptible animals and vaccination of at-risk animals. Vaccinated animals will not be subsequently slaughtered. Vaccinated animals intended for breeding, milking, or other purposes can be allowed to live their useful lives.

- *Emergency vaccination to live without stamping-out*. Vaccination is used without depopulation of infected animals. Vaccinated animals will not be subsequently slaughtered. This strategy is generally adopted when the disease becomes widespread and enough resources are not available for stamping out. This strategy will not be implemented at the start of the outbreak but may be adopted midway if the disease becomes widespread.

3. Factors Influencing Selection of a Response Strategy

Selection of a response strategy or strategies during an FMD outbreak is based on the following factors:

- *Impact of the Outbreak***.** The impact of the outbreak in terms economic losses, losses due to response measures, disruptions to trade, and other associated sectors with livestock industry.

- *Social and Diplomatic Issues*. Response policies selected should be socially, politically and diplomatically acceptable at state, national and international levels.

- *How Big is the Outbreak?* The number of animals, species and premises that are already infected, and the ones which are susceptible for infection or are at high-risk of infection will account for the scale of the outbreak.

- *Spread Rate*. The spread rate is a significant indicator of the scale of the outbreak in terms of number of premises and animals infected (Bates, Carpenter and Thurmond, 2003).

- *Availability of Quarantine Facilities*. The availability of FMD vaccines and other veterinary services is an important factor

- *Capability, Resources and Limitations in Implementing Response Strategies*. Readiness for swift response in terms of availability of resources and expertise and understanding of limitations can be a critical factor for selection of a response strategy.

4. Implementing a Response Strategy

During an outbreak, one or more of the response strategies may be adopted to control the spread of FMD. The strategy may vary for each geographical region, species, and other defining factors. The strategy to be implemented must be weighed in terms of the factors discussed above. Any response strategy requiring emergency vaccination requires the approval of the U.S. CVO in consultation with a SAHO. In the eventuality of FMD detection, the USDA and the affected states will work under a unified command to swiftly enforce a response strategy.

D. LITERATURE REVIEW

DEFRA (2002) gives an account of the results of the investigations conducted on the outbreak of the 2001, UK FMD epidemic. In the opening notes, the paper enumerates the difficulties experienced in establishing exact timelines for the outbreak. Uncertainties about parameters like the incubation period, first display of clinical signs, identifications and reporting of the disease add complications to the mathematical model. Therefore, the inputs as to when the infection entered a premise are based on an estimate either by the

farmers or by the veterinarians. The predictive capacity is directly proportional to the authenticity of the inputs received. The paper highlights the origin of infection and the possible causes that led to an inordinate delay in the detection of the disease. The huge economic impact of the outbreak reiterated the devastating capability of the world's most contagious disease.

Based on the background, several simulation models have been undertaken. Bates et al. (2003), evaluate several control scenarios during a hypothetical FMD breakout. Basic tools of baseline eradication strategy and control strategies such as slaughter or vaccination were dynamically simulated. Results of the study provided useful insight in understanding the advantages of various strategies for control and eradication of FMD. The study identifies that preemptive slaughter of the highest-risk herds and vaccination of all animals are important contributory factors that significantly reduced the size and duration of an epidemic. Preemptive slaughter and vaccination were identified as more economically viable strategies as against baseline eradication.

The 2001 epidemic was modeled in Uruguay using geo-referenced data (Chowell, Rivas, Hengartner, Hyman and Castillo-Chavez., 2005). The paper provides useful insight towards modeling techniques and its applications in disease simulation. The paper uses a least squares fit to study the epidemiological and control parameters and evaluates the impact of time delays on the implementation of movement restrictions. The paper concludes that secondary outbreaks can be triggered from long distance sparks of infection. These outbreaks are of higher intensity and take longer time for detection.

Carpenter et al. (2007) studies the impact of an introduction of FMD at the California State Fair. The spread was simulated through separate index cases at the fair. The model estimated with a probability of 0.8 that no animals would be clinically infected by day five. It is assumed that clinical signs of FMD would first be detected by the exhibitor with a high probability that it will not be further reported to the state veterinarian. The paper concludes that if FMD was introduced at the California State Fair, infection may go undetected till the animals leave the fair. The consequential outbreak would spread rapidly influenced by the unrestricted movement of the livestock and through indirect transmissions from humans, vehicles and fomites in contact.

Pineda, Carpenter, O'Brien and Thunes (2008) study the potential impact of an introduction of foot-and-mouth disease from wild pigs into commercial swine and dairy premises in California. The study uses a spatial stochastic simulation model to simulate epidemics of FMD. The paper concludes that the geographic region was a major discriminatory factor significantly contributing towards variance in epidemic duration, magnitude and infectivity of the outbreak. The paper acknowledges the rapidity with which the disease can spread over a large area. A statewide movement ban was identified as a significant strategy for reducing the spread of the disease.

Based on a simulated outbreak in California, a study was undertaken to analyze the epidemic and economic impact of the delayed detection of FMD (Carpenter et al., 2011). The economic impact was assessed for the entire U.S. The median economic impact was estimated to be in the range of $2.3–$69.0 billion, considering a detection window of 7 to 22 days. This study was instrumental in highlighting the importance of reducing diagnostic delay through sustained surveillance and control measures.

The extant Foreign Animal Disease Preparedness and Response (FAD PReP) materials have been revised and the USDA, APHIS has released an updated FMD Response Plan (USDA APHIS Red Book, 2012). The book illustrates the response goals and strategies and accounts for the logical progression for remedial actions that need to be prioritized for complete FMD eradication. We tabulate key definitions as defined by the USDA in Table 1 and Table 2 and provide a pictorial depiction of zones, premises and areas in Figure 6.

Table 1. The USDA APHIS provides the definition of premises, zones and areas and establishes the boundaries for standard reference throughout U.S. We tabulate the information provided in the USDA APHIS (2012) and define premises and zones with specifications in Table 1 and Table 2, respectively. A pictorial depiction of the areas is shown at Figure 6 (After USDA AHIS, 2012).

Premises	Definition	Zone
Infected Premises (IP)	Premises where positive case or confirmed positive case exists based on laboratory results, compatible clinical signs, FMD case definition, and international standards.	Infected Zone
Contact Premises (CP)	Premises with susceptible animals that may have been exposed to FMD, either directly or indirectly, including but not limited to exposure to animals, animal products, fomites, or people from Infected Premises	Infected Zone, Buffer Zone
Suspect Premises (SP)	Premises under investigation due to the presence of susceptible animals reported to have clinical signs with FMD. This is intended to be a short-term premises designation	Infected Zone, Buffer Zone, Surveillance Zone, Vaccination Zone
At-Risk Premises (ARP)	Premises that have susceptible animals, but none of those susceptible animals have clinical signs compatible with FMD. Premises objectively demonstrates that it is not an Infected Premises, Contact Premises, or Suspect Premises. At-Risk Premises seek to move susceptible animals or products within the Control Area by permit. Only At- Risk Premises are eligible to become Monitored Premises.	Infected Zone, Buffer Zone
Monitored Premises (MP)	Premises objectively demonstrates that it is not an Infected Premises, Contact Premises, or Suspect Premises. Only At-Risk Premises are eligible to become Monitored Premises. Monitored Premises meet a set of defined criteria in seeking to move susceptible animals or products out of the Control Area by permit.	Infected Zone, Buffer Zone
Free Premises (FP)	Premises outside of a Control Area and not a Contact or Suspect Premises.	Surveillance Zone, Free Area
Vaccinated Premises (VP)	Premises where emergency vaccination has been performed. This may be a secondary premises designation.	Containment Vaccination Zone, Protection Vaccination Zone

Table 2. Tabulation of terms related with Zones and Areas as defined by USDA APHIS (2012).

Zone/Area	Definition
Infected Zone (IZ)	Zone that immediately surrounds an Infected Premise. Perimeter should be at least 3 km (~1.86 miles) beyond perimeters of presumptive or confirmed Infected Premises. It will depend on disease agent and epidemiological circumstances. This zone may be redefined as the outbreak continues.
Buffer Zone (BZ)	Zone that immediately surrounds an Infected Zone or a Contact Premises. Perimeter should be at least 7 km (~4.35 miles) beyond the perimeter of the Infected Zone. Width is generally not less than the minimum radius of the associated Infected Zone, but may be much larger. This zone may be redefined as the outbreak continues.
Control Area (CA)	Consists of an Infected Zone and a Buffer Zone. Perimeter should be at least 10 km (~6.21 miles) beyond the perimeter of the closest Infected Premises. This area may be redefined as the outbreak continues.
Surveillance Zone (SZ)	Zone outside and along the border of a Control Area. Width should be at least 10 km (~6.21 miles), but may be much larger.
Free Area (FA)	Area not included in any Control Area.
Vaccination Zone (VZ)	Emergency Vaccination Zone classified as either a Containment Vaccination Zone (typically inside a Control Area) or a Protection Vaccination Zone (typically outside a Control Area). This may be a secondary zone designation.

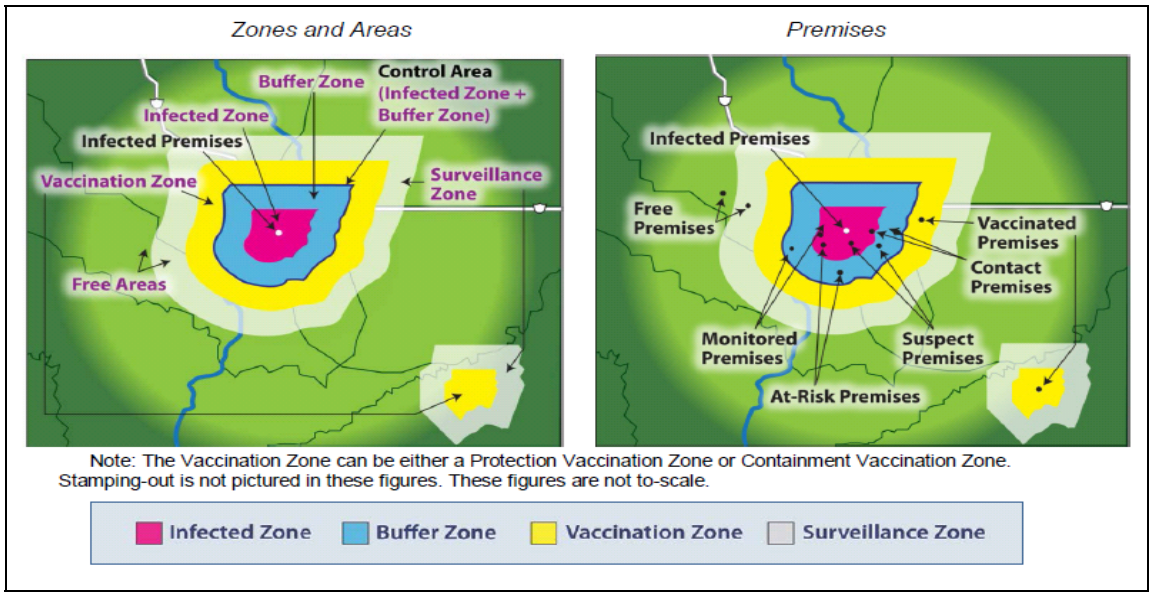

Figure 6. Pictorial Depiction of Premises Zones and Areas (From USDA APHIS, Red Book, 2012)

E. RESEARCH OBJECTIVE

1. Problem Statement

Given the susceptibility of an FMD outbreak in U.S. that may lead to extensive financial losses, we undertake simulation analysis using disease modeling software and experimental design for identification of factors contributing to the spread of the disease and evaluation of control strategies.

2. Research Questions

We use the outputs from our simulation and statistical analysis to answer the following research questions so as to provide additional insights for developing effective policies for controlling the spread of FMD in California.

a. Does the simulation of an FMD outbreak in California produce plausible outputs, in terms of numbers of animals infected, and impact of infection parameters on disease progression?

b. What are the disease spread parameters that significantly contribute to the outbreak? Is it possible to explain most of the simulation results by just a few parameters and their interactions?

c. Which are the critical control measures that can affect the disease progression? What are the effects of market, direct and indirect movements on the spread of the disease? Do movement restrictions reduce the size of the outbreak? If yes, then what is the smallest restriction that would be sufficient to reduce the spread?

3. Assumptions and Limitations of the Study

We assume that the outbreak is essentially caused by FMDV O serotype (as was the case for the UK FMD) and all the parameters, variables and conditions remain constant throughout the study (Brown and Deshpande, 2007). We also assume that all FMDV susceptible species are unvaccinated.

We limit our study to Zone 3 in Central California. Zone 3 is the subdivision of Central California as given in the California Coordinate System 83 (CCS83). Zone 3 is divided in counties as shown at Figure 7. We base our model parameters and output analysis on the inputs from subject matter experts and literature available on this subject. However, we do understand that inbound and outbound movement of livestock will take place between farms and markets beyond Zone 3. We include the coordinates of markets throughout the state of California. We do not model intra state movements of the livestock.

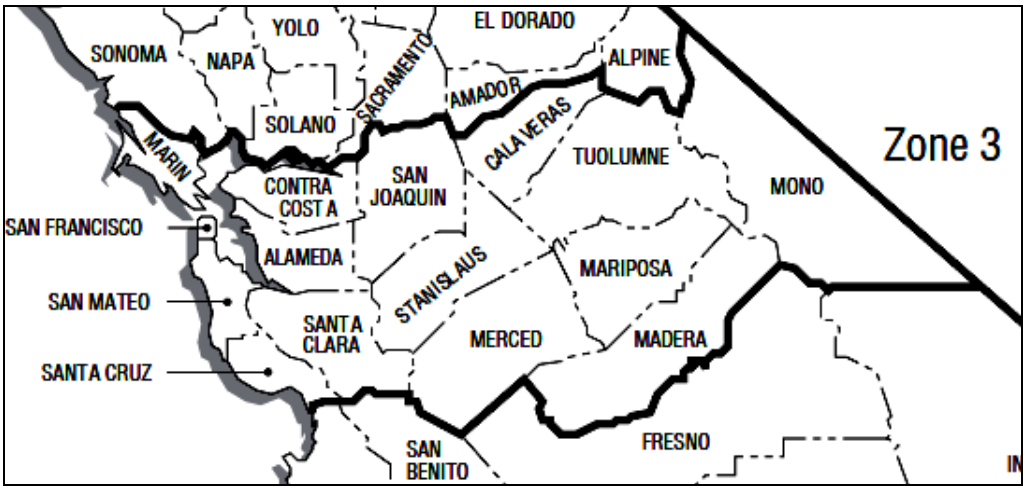

Figure 7. Map of Zone 3 in the California Coordinate System 83 (from California Department of Transportation, 2004). The map shows all the counties in the Zone 3.

II. METHODOLOGY

We simulate an outbreak of FMD across Zone 3 in Central California using the state of the art disease modeling ISP simulation package. In this Chapter, we explain the basics of the simulation software we employ, and the necessary disease and control parameterization.

A. INTERSPREAD PLUS–STOCHASTIC AND SPATIAL EPIDEMIC MODEL

We use ISP version 2.1.12.15 for the study. ISP is a stochastic spatial model of FMD written in C++ (Stevenson, 2003). The model uses geographic coordinates of farms and markets within a defined area or a control zone to create a spatial environment. Each farm is defined by the number and type of animals it contains. ISP uses a state transition model where the status of each farm at any given time can be one of (Stern, 2003 and Stevenson, Sanson, Stern, O'Leary, Moles-Benfell and Morris, 2007):

- *Susceptible*: Species present at a location are susceptible to infection.
- *Infected*: Species present at the location have already been exposed to infective agents. The disease is either incubating or clinical signs are visible.
- *Waiting and Processing*: Sub-categories of the infected and susceptible state include Waiting (farms are awaiting sanitary measures) and Processing (sanitary measures have been in force on location).
- *Not at Risk*: Sanitary measures render individuals incapable of becoming infected.
- *Depopulated*: A depopulated state implies that the location is no longer infectious as all the species have been removed from the location.
- *Vaccinated*: A vaccinated state implies that after a sufficient time has elapsed from the last vaccination, the location ceases to be susceptible and infectious.

ISP uses a simulation time step of one day. All time references in the model for input and output are in terms of days. The users define disease parameters through specifying probability distributions on the chance of occurrence of various events.

B. MODEL PARAMETERIZATION

This section briefly describes the various files that are used in ISP to set up the simulation model.

1. The Farm File

We modify the data set used in Axelsen (2012) to include only Zone 3 of Central California. The density of farms in Zone 3 is pictorially depicted in Figure 8. We observe that certain areas have a higher density of farms as highlighted in darker shades of green. Figure 9 depicts the distribution of different types of farms in Zone 3.

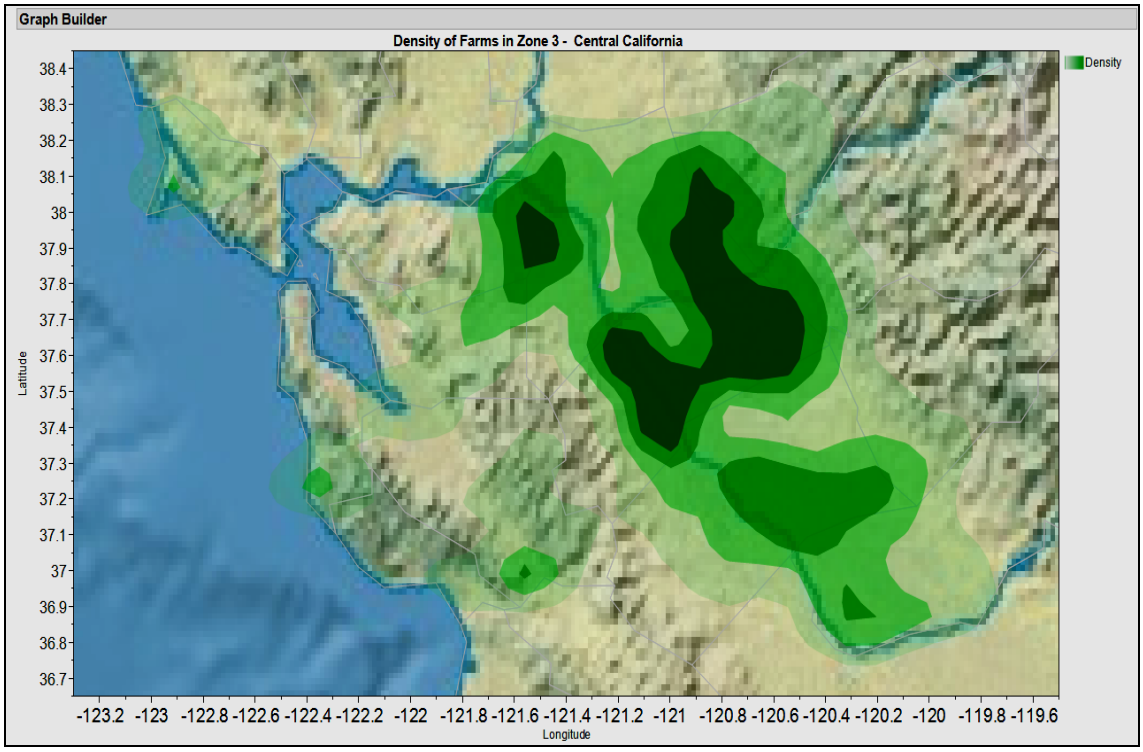

Figure 8. The density map of farms in Zone 3. The density index increases with lighter to darker shades of green. This map highlights that certain locations in Zone 3 have larger concentrations of farms highlighted in darker shades of green.

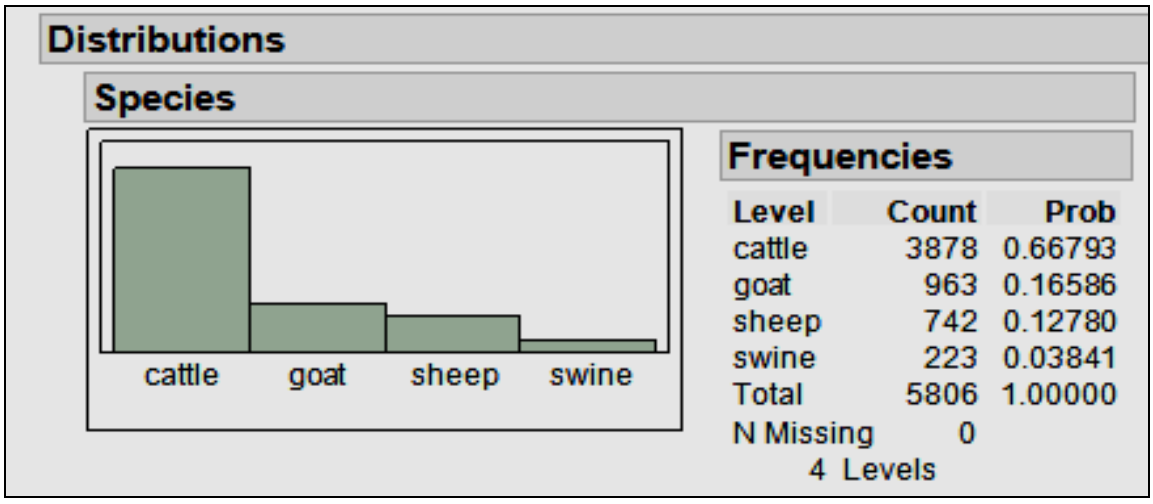

Figure 9. Histogram of types of farms in Zone 3. We observe that almost 66.7 % of the total number of farms are cattle farms and only 4 % of the total farms are swine farms in Zone 3. We highlight this observation because control measures such as dairy-like surveillance, which are implemented in cattle farms, are effective in Zone 3 (see Chapter IV).

ISP carries out the FMDV spread simulation through a heterogeneous population of spatially defined farms (Moles- Benfell, 2007). The farm file defines the attributes of the farms under study. Each farm is defined in terms of its location in latitude and longitude, size of herd population, and the type of livestock. Coding nomenclature for farms is retained from Axelsen (2012).

Table 3. A section of the farm file that is used in the model is tabulated below. Each row is dedicated to a separate farm. The colums define the attributes of the farm.

Type	Premises	ID	Size	FIPS	Lat	Long	Zone	Cattle
33	Dairy(L):3429	3429	506	6099	37.67433	120.733	3	506
33	Dairy(L):3430	3430	512	6099	37.33906	121.063	3	512

2. Control File

This is the basic file that sets up the simulation in ISP. ISP has a graphical user interface which is used to input the disease parameters and the geographical area under study. It is mandatory to define the population at risk, the initial subset of the population

that is infected, and the spread mechanism of the disease. The control file also assigns the number of replications and terminating conditions. We run 50 replications of our simulation model. The terminating condition is set as 40 days from the day of initial infection. The control file also allows the user to define additional transition states, on top of those described in Section B. We retain the same user-defined states as Axelsen (2012), pp. 31–32.

3. Epidemic History

The epidemic history gives the initial condition of the infection. We use the term '*infected'* to indicate the day when the premise is infected. The term '*clinical signs*' indicates the day of onset of clinical signs. '*Detected'* indicates the day when the disease is diagnosed. For the simulation to start, we define a subset of a population that is initially infected by the disease. The model then simulates the spread of the disease in accordance with the parameters specified in the control file.

4. Initially Infected Subset

For our model we created four starting scenarios to cover a range of infection probabilities.

- *Port_SF*: We simulate that a farm in the port of San Francisco is targeted by terrorists. The San Francisco port was chosen due to its impact in the livestock industry and its prominence in the state of California. A beef farm is randomly infected in this region and the impact is studied through the simulation.

- *High_Animal*: We rank the farms according to the number of animals within 10km of the farm, and originate the infection in a farm that is at or above the 90th percentile in the ranking.

- *High_Premise*: We rank the farms according to the number of farms within 10km of the farm, and originate the infection in a farm that is at or above the 90th percentile in the ranking.

- *MarketStart*: We originate the infection in a market in Zone 3 to study the effect on the spread of FMDV due to movement of livestock from market to farm and market to market.

C. SPREAD MECHANISM AND SELECTION OF DISEASE PARAMETERS

After we define the initially infected and susceptible population, ISP simulates the spread of infection. Our parameterization does not include airborne spread, only spread based on movement and proximity.

1. Movement Type

Movement type refers to a movement that occurs from farm to farm, farm to market, or market to farm. We include direct, indirect and market movements in our model. We modify the model used in Axelsen (2012) to include only those movements identified as significant contributors to the spread of the disease (Axelsen, 2012, Figure 10, p. 51). The Appendix lists the parameters included in our DOE. Movement types not included in our DOE are removed from the control file. In addition, we add farm to market movement in the DOE to study its effect in greater detail. For the retained movement types, we also retain the associated parameters. The simulation assumes that infected animals do not transmit the virus during movement, only at their destination.

2. Local Spread

Local spread is a significant factor for the spread of FMDV**.** Stevenson (2007) defines local spread as "the mean disease spread between livestock holdings when there is no clear linkage other than a geographical proximity spread mechanism to model short distances." The likely causes of the spread could be an aerosol dispersion of infectious agents, undocumented movement of fomites and neighbor-to-neighbor across the fence contact (Stevenson et al., 2007).

During the 2001 U.K. FMD outbreak, the source of infection for 1,802 out of 2,030 infected premises was attributed to local spread (Stevenson, 2007). The study revealed that the source premises were those infected premises that were within 5 km of

the recipient premises. We reduced the distance up to which the FMDV can travel due to local spread to 5,000m based on recommendations in Axelsen (2012).

3. Infectivity

Stevenson et al. (2007) defines infectivity to be "a factor that determines the behavior of the disease, once individuals at a location become infected." It includes the length of time from infection to the onset of clinical signs (incubation period) and the length of time from infection to the onset of infectiousness. Intuitively, infectivity defines the likelihood that an infected farm spreads the disease, and the likelihood that a susceptible farm becomes infected.

4. Disease Control Parameters

We use various options such as surveillance, movement restrictions, vaccination, tracing and depopulation measures for restricting the spread of the disease in our model. We use similar definitions and terminologies for all control parameters as explained in (Axelsen, 2012. p. 41)

a. Zonal Control

Zonal boundaries of adjoining states of Zone 3, i.e., Zone 2 and Zone 4 are included in the model for enforcing control measures. Though Zones 2 and 4 only include markets in our model, surveillance and control in those markets may significantly reduce the spread in Zone 3.

b. Surveillance

Upon transition from an infected state to a detected state, control measures may be applied for limiting the spread of the disease. Surveillance zones may be enforced in a buffer area around an infected and detected premise, as described in Figure 6. Surveillance cycle begins at the start of the simulation run when the farm gets infected. Each farm is assigned a probability for inclusion in the surveillance list. We model the distribution describing the number of time periods that will pass between visits to a farm

and the periods from when the visit occurred to when that farm will receive the detected state as a Poisson process. For our model, detection is based on the clinical signs.

c. Resources

A resource within ISP includes all of the state veterinary services that can be called upon to handle epidemics of various sizes and durations. There are two main types of resources, vaccination resources and depopulation resources. Depending on the availability of resources, farms are processed faster or slower for vaccination and depopulation.

d. Depopulation

This section of the ISP model is used to specify the depopulation strategy as discussed in Chapter 1, Section C. We choose to depopulate only those premises that have been detected with the disease. We do not model alternative preemptive depopulation in zones as it is against USDA guidelines (USDA APHIS, The Red Book, 2012).

e. Vaccination

The vaccination section of the ISP model enables the user to define which farms require vaccination. The type of species to be vaccinated is specified. For our model, we specify that the vaccination control will be activated for all farms that are detected with FMDV. The vaccination resources are available from the start of the simulation. We also specify an immunity value that is applied to the farm's resistivity to infection. Vaccination strategy is taken from the USDA guidelines as discussed in Chapter 1, Section C.

f. Tracing

Tracing can be of two types, *backward* or *forward,* depending on what event or period is being used to track the contacts that cause the spread of the virus.

Tracing is said to be backward tracing if it involves studying past events to identify contacts that occurred between the estimated date of infection and the start of the epidemic.

Tracing is said to be forward tracing when it involves identifying contacts made by the detected farm during the infectious period. This ensures identification of farms potentially exposed to infection, and therefore likely to develop the disease (Stevenson et al., 2007). Interview of the staff of the detected premise provides useful information for tracing. ISP has both forward and backward tracing features. For our model, we use forward tracing as we set the reference for starting the tracing activity when the first infected farm is detected. We also assign a probability that the specified movement type or route in the specified direction may be forgotten by the farmer and therefore may never be traced. We retain the tracing parameters used in Axelsen (2012).

g. Movement Restrictions

Once infection on a premise is detected, movement restrictions may be enforced. As the days from detection increase, the movement restrictions become stricter. Stevenson et al. (2007) gives an estimate that from 0 to 10 days after detection, movement restrictions may be imposed. It is expected that up to 10 days, the movements of animals, humans and fomites will be restricted by about 80% and from day 10 onwards, as the effectiveness of controls increase, probability of movement restriction may increase up to 100%.

For our model, we impose movement restriction when the first infected farm is detected. We specify the type of movement, and the specific zones and areas in which the restrictions would be applied. These restrictions are continued throughout the simulation.

D. MODELING ASSUMPTIONS AND LIMITATIONS

We make the following modeling assumptions which remain present throughout the study.

- The strain for the FMD Virus is FMDV O (as was the case for the 2001, U.K. FMD outbreak).
- All animals are considered to be unvaccinated, and are susceptible to infection initially.
- Each farm has only one type of species.
- Following the construction of ISP, between-herd disease progression is the focus of the simulation, as opposed to within-herd progression.
- The data set pertaining to Zone 3 is plausible (Axelsen, 2012). The locations of farms and markets are representative of the real world.
- Model parameters, variables and conditions remain constant throughout the simulation (Brown et al., 2007).

Our model is constrained by the following limitations:

- We terminate simulation at the 40th day from the start of the simulation.
- We limit the range of high and low values in the DOE for probability of spread, distance covered, and spread rate based on past work (Axelsen, 2012). We do not consider parameter values beyond this range for our simulation runs. We could not physically validate the spread parameters and accuracy of the data set by carrying out a field trip to farms and markets in Zone 3 of Central California.

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III. DESIGN OF EXPERIMENT

Design of Experiments (DOE) techniques enable simultaneous evaluation of individual and interactive effects of numerous factors that could affect the output of a simulation model. DOE gives useful insight into the interaction effects of the design elements and provides an organized approach to data gathering (Jsifri, 2009). We use statistical tools such as regression and partition tree models to obtain valuable information from our simulation runs.

A. METHODOLGY FOR CREATION OF THE EXPERIMENTAL DESIGN

The broad aim of the model is to simulate the spread of FMD in a regional geographical set up and to identify critical disease and control parameters. As a starting point, we use the parameter settings for 46 out of 72 parameters that are the most significant in Axelsen (2012). We adopt the recommendations of Axelsen (2012) and compare our zonal results to the state-wide model of Axelsen. Following a key recommendation, we add market movement in our zonal model as we expect this parameter to be a significant contributor towards the spread of the disease.

We focus on the most explanatory parameters out of the 46 initial parameters using regression analysis and a Nearly Orthogonal Nearly Balanced Mixed Design (from the Simulation Experiments and Efficient Design (SEED) center for data farming, Naval Postgraduate School, Monterey). Simulations on the design points are run in parallel on a cluster of 52 computers. Before we run the simulation for 50 replications on each design point, we carry out plausibility testing of the model. We formulate MOEs for quantitative analysis of the simulation output.

The design is called nearly orthogonal as it has very low absolute pairwise correlation between any two design columns. The maximum absolute pairwise correlation of the design used is around 3.56%. Nearly balanced means that for any factor column, the number of occurrences of each factor level is nearly equal (Vieira, 2012). Each row of the design matrix represents one simulation run and is designated as a *design point*.

Every column represents a certain parameter in the simulation model, called a *factor*. For our model, all factors that affect FMDV infection, disease spread and control are arranged in columns for the experimental design. These factors have different possible values called levels. The NOB Mixed 512 design worksheet has nearly independent first-order factor effect estimates (Vieira, 2012).

We assign the upper and lower bounds for each of the factors in the experimental design along with the level of decimal precision. In the experimental design, the last two factors, Resource 1 and Resource 2 are dependent on the time when the use of the resources commenced and are therefore correlated.

We create a separate excel spreadsheet where each row indicates one starting scenario and cross it with the 512 design points. This multiplies 512 design points with four starting scenarios to produce a total of 2,048 total design points with the name of the starting scenarios in the first column. We replace the header rows to indicate the lower bound values, upper bound values, number of decimal points, discrete levels and the factor names. The above methodology creates the design of experiment required for the simulation run. We carry out 50 replications in total by creating 102,400 design points. A few of the initial rows and columns of the DOE are tabulated as Table 4.

Table 4. A section of the DOE with four rows for each starting scenarios. Each row represents one design point. The columns are the factors used in the model. The factors could either be categorical, continuous or discrete. We use the NOB_Mixed_512DP worksheet from Naval Postgraduate School SEED Center to create the DOE.

low level	x	0	0	0.01
high level	x	1	0.99	0.15
decimals	x	0	2	4
factor name	EpidemicHistory:StateFileName	Vaccination1	MovementRestriction3	MovementType1
1	.\STATE_Animal_High.txt	1	0.99	0.0201
2	.\STATE_Animal_High.txt	0	0.99	0.079
3	.\STATE_Animal_High.txt	0	0.99	0.0604
4	.\STATE_Animal_High.txt	0	0	0.0727
513	.\STATE_Port_SF.txt	1	0.99	0.0201
514	.\STATE_Port_SF.txt	0	0.99	0.079
515	.\STATE_Port_SF.txt	0	0.99	0.0604
516	.\STATE_Port_SF.txt	0	0	0.0727
1025	.\STATE_Premise_High.txt	1	0.99	0.0201
1026	.\STATE_Premise_High.txt	0	0.99	0.079
1027	.\STATE_Premise_High.txt	0	0.99	0.0604
1028	.\STATE_Premise_High.txt	0	0	0.0727
1537	.\STATE_MarketStart.txt	1	0.99	0.0201
1538	.\STATE_MarketStart.txt	0	0.99	0.079
1539	.\STATE_MarketStart.txt	0	0.99	0.0604
1540	.\STATE_MarketStart.txt	0	0	0.0727

B. VALIDATION OF THE DESIGN OF EXPERIMENT

We expect to see good space-filling properties as we have used a NOLH based experimental design. We expect to see a comprehensive coverage of the input space due to the space-filling attribute of the NOLH design. We validate this attribute of our experimental design and observe that we have comprehensive coverage of the input space as shown in Figure 10.

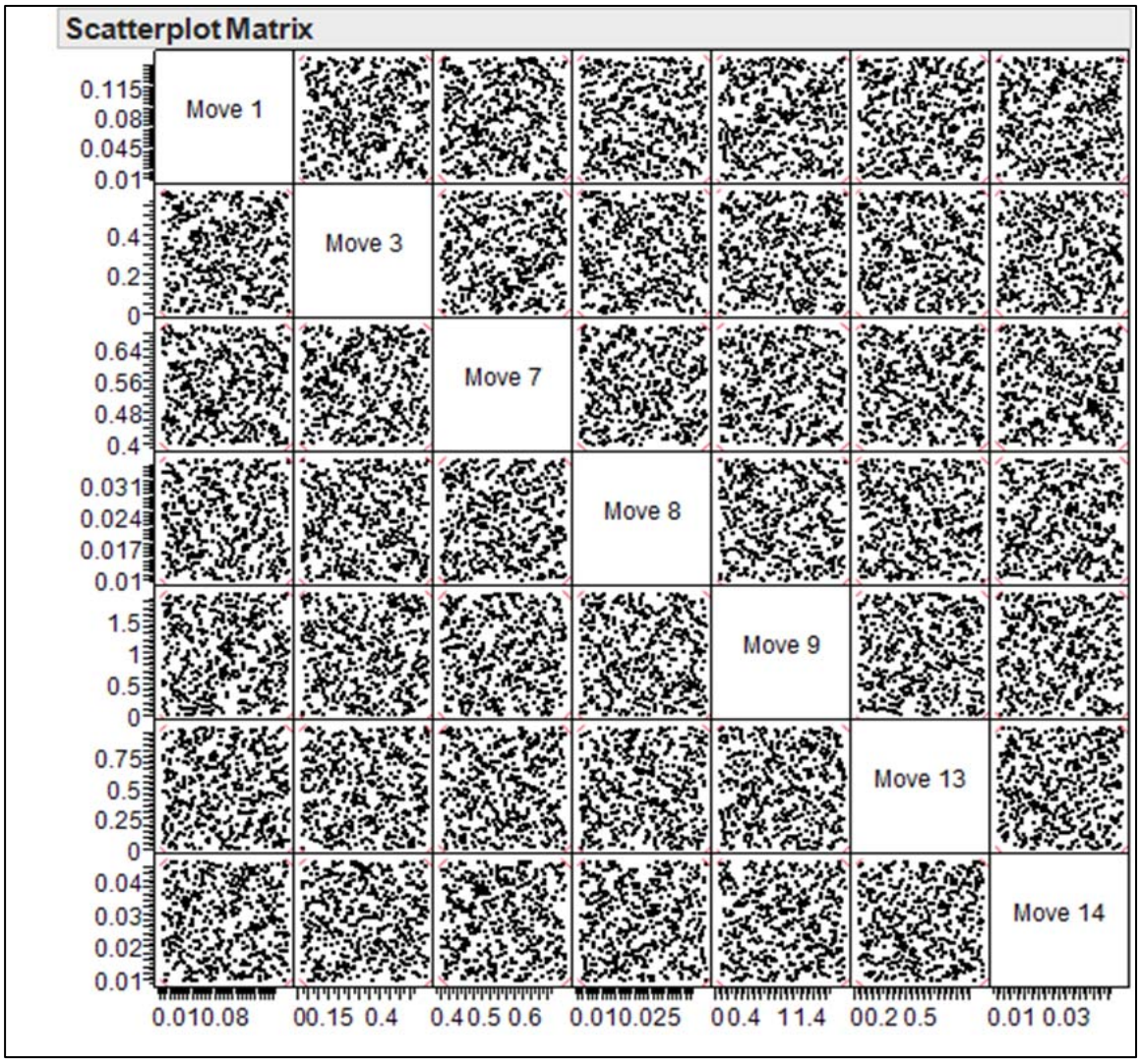


Figure 10. We present a section of the scatter plot of the correlation matrix and observe the space-filling property of the design of experiment. We observe that we have a comprehensive coverage of the input space which validates our experimental design.

Next, we check the correlation between the various input parameters. If the DOE was correctly formatted, then we expect to see negligible correlation amongst the input factors. Figure 11 shows the correlation among the input parameters.

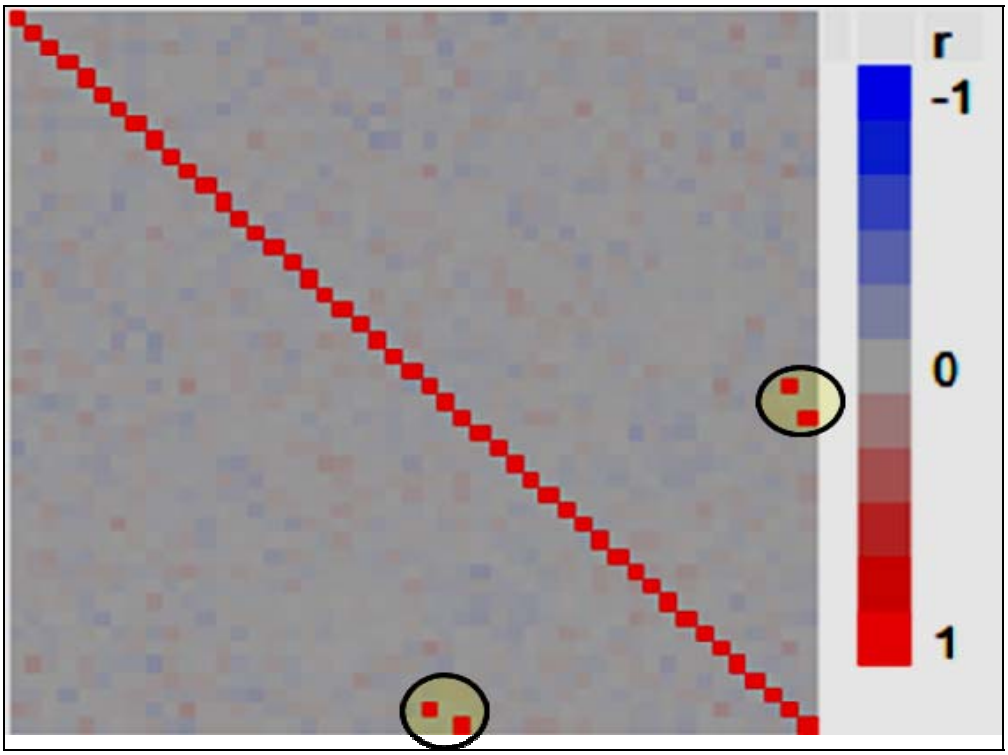


Figure 11. Correlation diagram of all the input factors. As seen, there is almost negligible correlation amongst the input variables except for the two parameters as shown in the circle which are dependent on other resource utilization factors. We observe a maximum absolute correlation of about 2.5% among the independent variables.

Figure 11 indicates that there is indeed very low correlation, almost negligible, amongst the input parameters. Factors indicating the time period when resources would be available for full utilization do come up with higher correlation values as they are linear transformations of other factors. We plot the histogram of the correlations amongst the factors and summarize it in Figure 12.

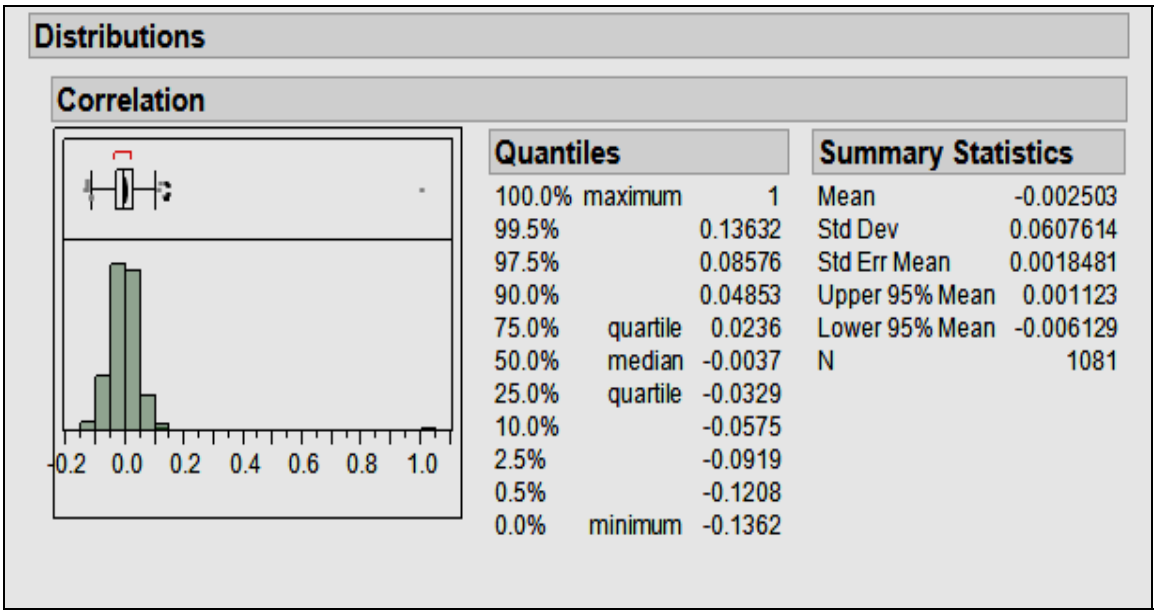


Figure 12. Histogram of correlation among the input variables. We observe that the mean value is -0.002 which indicates almost negligle correlation.

We observe a maximum absolute correlation of about 2.5% among the independent variables. Based on these findings, we conclude that our experimental design is appropriate for analyzing our scenario.

IV. DATA ANALYSIS

We set up the simulation at the SEED center and carry out a sanity check by running two replications of the model for each design point. Each replication of 2,048 design points took an average time of about 2.5 to 3 hours to run. This gave us an approximate idea that the whole simulation for 50 replications would take around 125–150 hours or approximately 5–6 days to run.

A. PLAUSIBILITY TESTING

Our main aim of the plausibility testing is to check whether the model is establishing the correct relationship between the cause and the effects, i.e., whether we see the expected impact of our chosen factors on our response variable. We use infected number of cattle as our response variable and study the impact of various input factors on the response variable. Figure 13 shows the relationship between the inputs and the response variable.

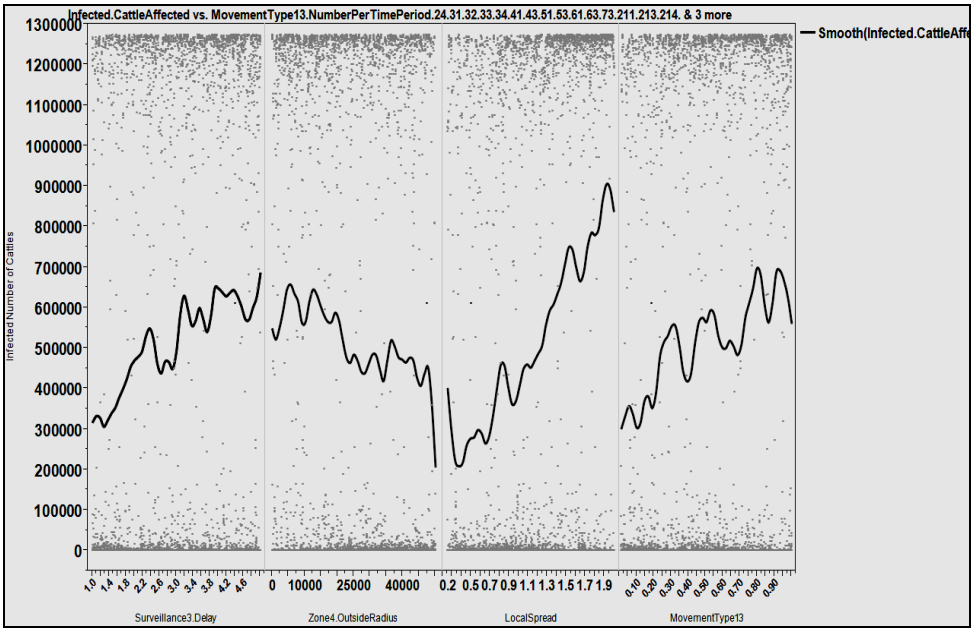


Figure 13. Plot depicting impact of factors on the number of cattle infected. On the X-axis we have the factors contributing to the spread of the disease and on the Y-axis we have the response variable. The smoother line indicates the effect of the factors on the response variable.

We observe number of cattle infected increases as the surveillance delay increases. A similar but more prominent effect is seen as the local spread multiplier increases, i.e., when the distance to which the virus can travel due to local spread increases. The number of infected cattle also increases as the probability of market movement increases. However, when we enforce control measures, the number of infected cattle decreases when the radius of the surveillance zone increases. We observe that factors are having the expected impact on the response variable. Based on the observations above, we conclude that our model is plausibile.

B. MEASURES OF EFFECTIVENESS

The main aim of the simulation study is to identify factors that can either be controlled or restrained to reduce the spread of the disease. We identify measures of effectiveness to help us quantify the effect of disease and control factors. The measures of effectiveness (MOEs) we consider are:

- *Detection Time*: OIE (2012) highlights that effective surveillance, early detection and early warning are instrumental in reducing the spread of FMD. This measure of effectiveness indicates the time duration between the start of the infection, i.e., when the simulation starts with a trigger from the starting scenario, to the time when the disease is detected at a farm.

- *Number of Infected Farms*: DEFRA (2002) gave useful insight on the scale of the 2001, U.K. FMD outbreak and how it was related to the number of infected farms. This MOE counts the number of infected farms during the simulation.

- *Number of Infected Cattle*: Initial exploration of the data set highlighted that cattle density was highest in farms in Zone 3 of Central California (refer to Figure 9). We also observed that spread of the disease in cattle was strongly correlated with the spread in other species as shown in Figure 14. Correlation in excess of 0.98 between species indicates that the results for cattle would also be applicable for other species. We use the number of cattle infected as a MOE to

study the effect of control options in reducing the spread of FMDV in cattle. We generalize those measures for all the species.

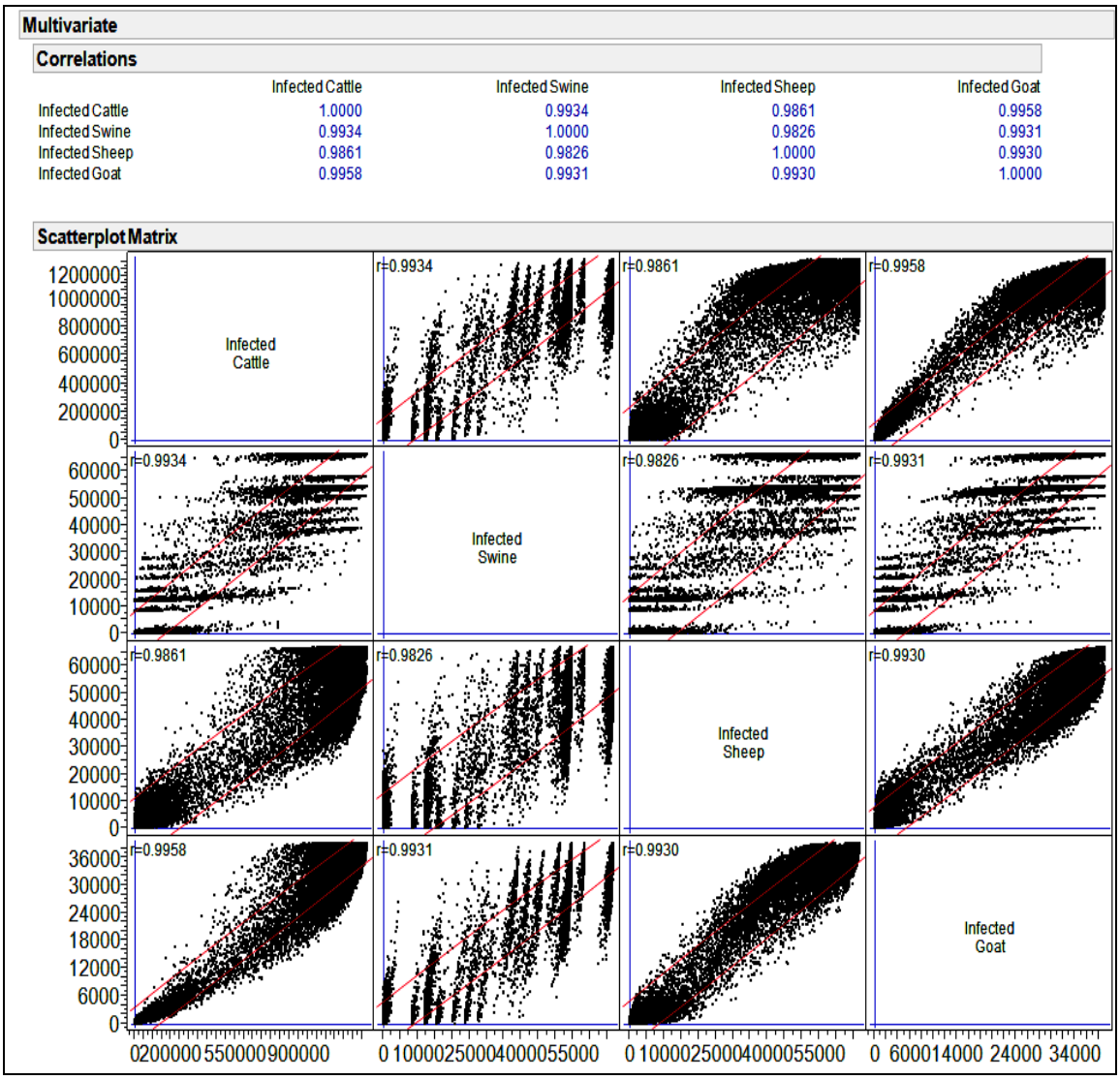


Figure 14. Scatterplot of the mean number of animals infected during the simulation run. The plot indicates high correlation among the number of cattle infected with the number of other species infected.

We use the mean of the 50 simulation runs for these MOEs. This reduces the size of the output file from 102,400 data points to 2,048 means of 50 data points. This method helps in achieving an approximate normal distribution for the mean value of the MOEs by employing the Central Limit Theorem. We observe in Figure 15 that the MOEs other

than detection time are highly positively correlated with each other. This implies that the independent regressors will have similar impact on these MOEs except on detection time.

Correlations

	Infected.CattleAffected	DetectTime	InControlArea.CattleAffected	Infected.FarmsAffected
Infected.CattleAffected	1.0000	-0.1315	0.8778	0.9978
DetectTime	-0.1315	1.0000	-0.1420	-0.1349
InControlArea.CattleAffected	0.8778	-0.1420	1.0000	0.8760
Infected.FarmsAffected	0.9978	-0.1349	0.8760	1.0000

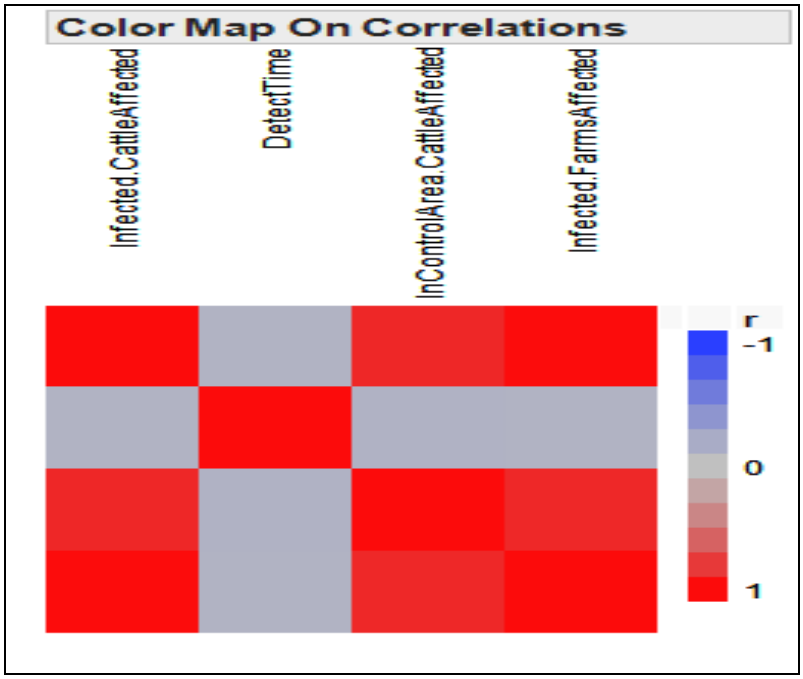


Figure 15. Color map of correlations between the MOEs. The range of correlations is from -1 to 1. The map shows that all the MOEs except detection time are highly positively correlated indicating similar responses to various independent regressors.

We initially choose one factor that is expected to have a large contribution on the spread of FMDV and study its effect on our chosen MOE. We expect to see similar effects on all our MOEs except detection time. Figure 16 shows the effect of market movement on all our MOEs. The smoothers for each graph indicate that market movement has similar effect on all our MOEs except detection time. The density index

indicates the concentration of observations for the given MOE. We include all three MOEs in our study so as to cater for a wider range of statistical inference that may look at either farms infected or animals infected.

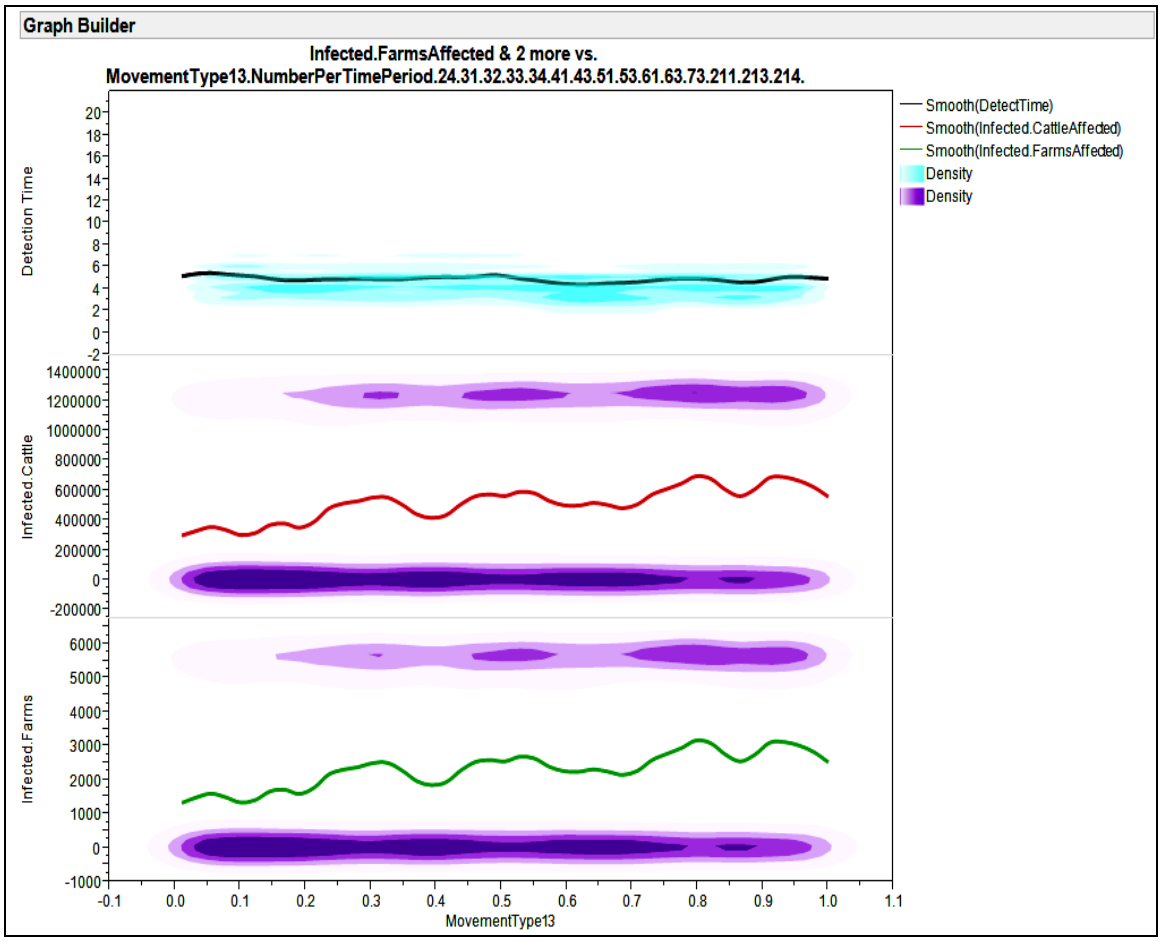


Figure 16. Graph depicting the effect of market movement on the three MOEs. On X-axis we have the probability of market movement between zero and one and on Y-axis we have the mean values of the three MOEs. We see that the effect of the independent variable is approximately constant for the detection time MOE and is similar for the other two MOEs, i.e., number of infections for both farms and cattle is increasing with the increase in the probability of the market movement.

C. MULTIPLE REGRESSION MODEL

We use a multiple regression model to answer our second research question, i.e., is there a significant relationship between the response variable and one or more of the factors? The model has the basic form as indicated by the equation below (Faraway, 2002):

$$Y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \ldots + \beta_k x_{ik} + \varepsilon_i \quad for \; i = 1, \ldots, n$$

where,

Let Y_i be the dependent response random variables. We study our chosen MOEs as the dependent response random variables one at a time.

Let x_i be the independent regressors or input factors. In our study, these are the disease and control factors.

Let β be the coefficients of independent predictors that are nonrandom unknown quantities. β_0 is the intercept term.

Let ε_i be the errors terms which are random variables. They are typically modeled as independent and identically distributed and are assumed to have normal distribution with zero mean and a constant standard deviation.

1. The Basic Model

We use our MOE of infected number of cattle as the response variable and carry out a linear regression with all the independent factors in the model. We observe that the model has an R^2 value (or a coefficient of determination) of 0.699 and an adjusted R^2 value of 0.6918 which means that the model can explain approximately 70% of the variability in the data. We carried out model diagnostics using the plots as shown in Figure 17.

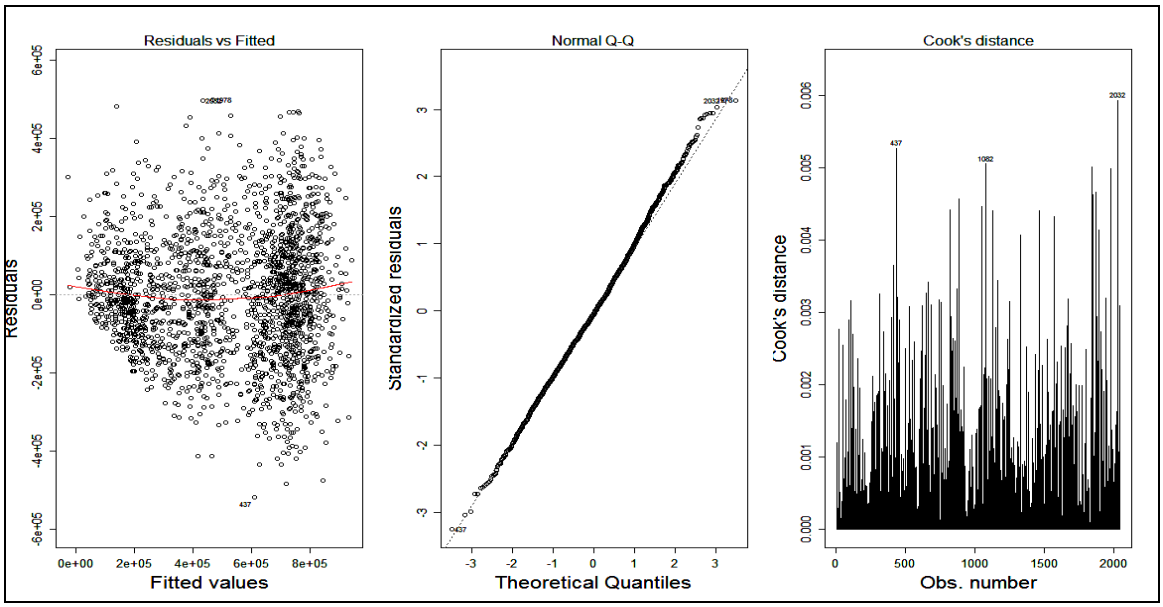


Figure 17. Diagnostic plots for the multiple regression model. Looking at the residual vs fitted plot we can say that there is nonconstant variance or heteroscadaticity in the model. The normal quantile plot indicates that the errors are almost normally distributed. None of the Cook's distance values (Faraway, 2012) are more than one which suggests that there are no influential points.

Heteroscedasticity is expected in our simulation model due to the large difference among the sizes, i.e., the number of animals, in each farm. The mean of the error terms, however, are driven by the Central Limit Theorem, so we expected the errors to be almost normally distributed. We carry out a Box-Cox transformation as shown in Figure 18 for the response variable to correct the heteroscedasticity and observe that a square root transformation may work for the response variable.

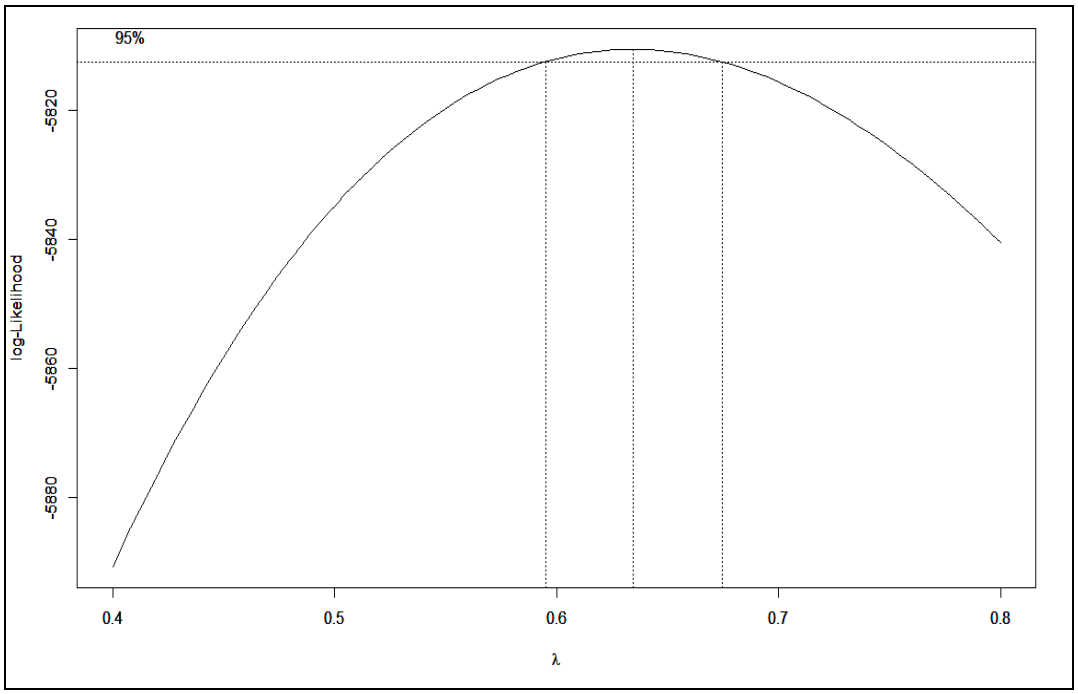


Figure 18. A graph showing Box-Cox transformation of the response variable , i.e., the number of cattle infected. We observe that the lambda value is between 0.5 and 0.7 indicating a requirement for a square root transformation.

We fit a model with the square root of the response variable and all the main effects in the model, and observe that the problem of non-constant variance is resolved as seen in Figure 19. The adjusted R^2 value also goes up from 0.6918 to 0.714.

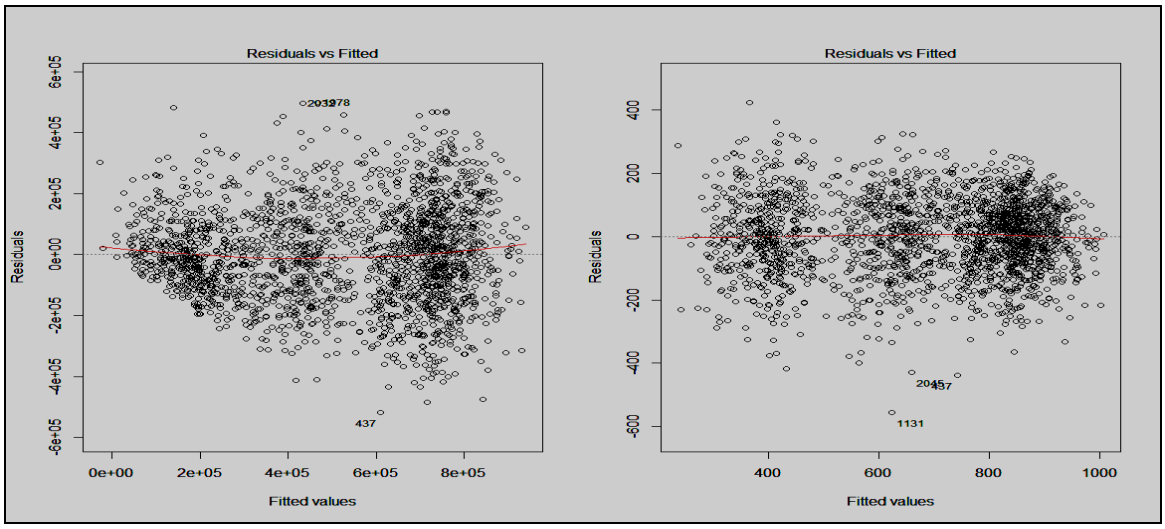


Figure 19. Graph of residuals against fitted values. The left graph is for the mean number of cattle infected without the square root Box-Cox transformation and to the right we have the graph with the square root transformation. We can see that the problem of heteroscedasticity appears to be resolved.

Since we used an NOLH experimental design, we are sure that the autocorrelation is low among the factors. Nonetheless we carry out a Durbin Watson test for reconfirmation that the autocorrelation is zero. The Durbin Watson statistic value of the test is 1.9315 with a p-value of 0.8096 which is higher than $\alpha = 0.05$. Thus, we say that we do not have sufficient evidence to reject the null hypothesis that the autocorrelation is zero.

2. The Saturated Model

Gerbier (1999) studied the interaction effects of various factors with a main emphasis on the effect of animal density on FMD spread. We develop an understanding that the model may require higher order terms and interaction effects amongst the predictors. Validation of all the assumptions enables us to carry out hypothesis tests and ANOVA tests. We fit a model with all the interaction effects and compare with a model without interaction effects. We hope to see the adjusted R^2 improve when interaction effects are included. The ANOVA p-value is 2.2e-16 which is much less than the significance level of $\alpha = 0.05$, thus we reject the null hypothesis that the unsaturated

model is better and say that interaction effects provide an improvement to the model. The model with interaction effects has an adjusted R^2 value of 0.8456.

Similarly we add nonlinear effects, i.e., quadratic and cubic effects of the terms in the model. We carry out a stepwise regression control and minimum BIC method of selection of variables. We see that the quadratic term for market movement and cubic term for local spread are also significantly contributing to the model. The saturated model with interaction and non-linear terms has an improved adjusted R^2 value of 0.8571. The statistics for the saturated model are shown in Figure 20. We present the first 20 factors in the order of their significance level in Table 5 and observe that interaction effects also appear in the list.

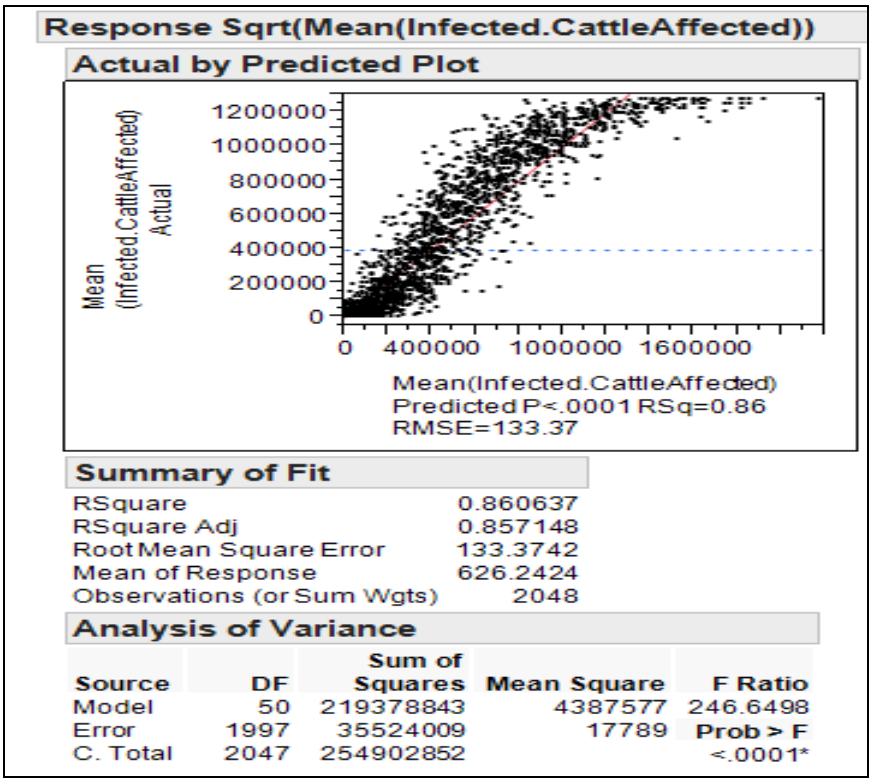


Figure 20. Graph highlighting the statistics of a model including interaction, quadratic, and cubic effects. We observe that when we include interaction effects, quadratic and cubic effects, the R^2 value goes up to 0.8606. The analysis of variance p-value is less than 0.0001 and shows that there appears to be significant differences in the means of the different models.

Factors with a high t-ratio as shown in Table 5 contribute more towards the explanatory power of the model. We use a partition tree in section D of this chapter to quantify the contribution of factors towards the overall explanatory power of the model. The major contributors for the number of cattle infected are the epidemic history, local spread, market movement type 13, surveillance delay in dairy-like farms, Zone 4 boundary, indirect movement type 15, market movement restriction and depopulation resources. We carry out sensitivity analysis for the significant contributors and highlight their effects in section C (4) of this Chapter.

Table 5. The table highlights sorted order of significance with which a factor contributes towards the response variable, i.e., the number of infected cattle. We see that epidemic history, local spread multiplier and market movement are the biggest contibutors to the disease.

Term	t Ratio	Prob>|t|	t Ratio
EpidemicHistory.StateFileName[.\STATE_Port_SF.txt]	-58.33	<.0001	-58.33
LocalSpread1.Multiplier	52	<.0001	52.00
EpidemicHistory.StateFileName[.\STATE_Animal_High.txt]	36.77	<.0001	36.77
MovementType13	26.22	<.0001	26.22
AllMovements.MovementDistance	23.33	<.0001	23.33
Surveillance3.DelayToDetection.GeneralSurv_Dairy_before	22.15	<.0001	22.15
MovementType15	19.85	<.0001	19.85
Zone4.OutsideRadius1.SurvZone	-19.68	<.0001	-19.68
MovementRestriction3.ProbMovementRestricted.MarketMvmt[0]	18.7	<.0001	18.70
Resource1.PerTimePeriod	-17.85	<.0001	-17.85
Resource1.TimePeriodStop1.Depop	14.83	<.0001	14.83
EpidemicHistory.StateFileName[.\STATE_MarketStart.txt]	-10.49	<.0001	-10.49
AllMarkets.ProbabilityOfTransmission	7.99	<.0001	7.99
MovementRestriction3.ProbMovementRestricted*(MovementType13)	7.73	<.0001	7.73
(LocalSpread1.Multiplier-1.125)*(Resource1.PerTimePeriod-1.125)	7.32	<.0001	7.32
(MovementType13)*(LocalSpread1.Multiplier-1.125)	-6.93	<.0001	-6.93
Surveillance1.VisitFrequency.GenSurv	6.35	<.0001	6.35
AllFarms.ProbabilityOfTransmission	6.01	<.0001	6.01
(Resource1.PerTimePeriod-1.125)*(Surveillance3.DelayToDetection.GeneralSurv_	5.61	<.0001	5.61
(LocalSpread1.Multiplier-1.125)*(Resource1.TimePeriodStop1.Depop-17.5)	-5.47	<.0001	-5.47

3. Metamodel

We present two separate multiple regression models that use a smaller number of factors without losing the explanatory power. This approach provides more flexibility in carrying out detailed analysis of reduced subset of the problem. The first model is applicable to all the MOEs except detection time. We present a separate model for detection time as it is not strongly correlated with other MOEs.

a. MOEs Other than Detection Time

This model is applicable to all MOEs except detection time. Given the costs involved in analyzing a vast number of factors, we seek to reduce the size of the model without degrading the predictive capacity. We use the adjusted R^2 method to identify what combinations of factors are contributing most to the basic model. We observe in Figure 21, that the adjusted R^2 almost flattens from eight to ten factors. This gives us an indication that main effects, interaction, quadratic and cubic effects of only eight to ten factors out of 47 may actually contribute towards the explanatory capacity of the model for a given MOE. This aligns with the 80/20 Pareto's principal. Koch (2012) explains the Pareto's 80/20 principal as:

"There is an inbuilt imbalance between causes and results, inputs and outputs, and efforts and rewards. Typically, causes, inputs or effort divide into two categories (a) the majority, that has little impact and (b) a small minority that have a major, dominant impact."

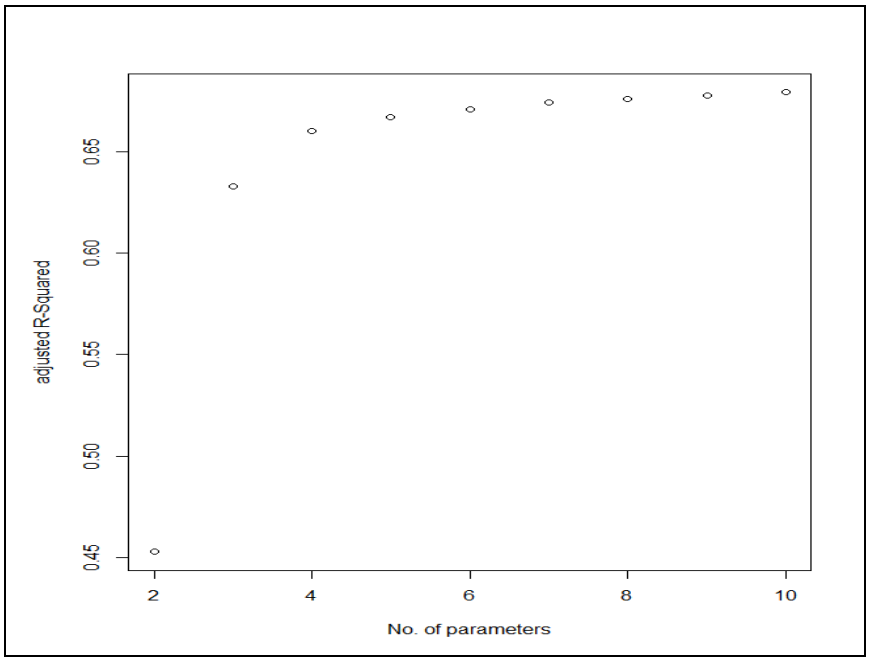


Figure 21. The adjusted R^2 plot for the choice of factors to be included in the model. We observe that there only eight to ten factors that are significantly contributing to the predictive capacity or the variance explanatory power of the basic model. On gaining insights, we add factors in the order of Table 5. For a given set of factors, we use a model that includes all interaction, quadratic, and cubic effects.

The model with highest adjusted R Squared value includes the following factors: epidemic history, movement restriction for all markets in Zone 3, surveillance delay in dairy-like facility, depopulation resources, local spread distance multiplier, all movements distance multiplier, market movement type 13, direct movement type 3 in sheep from farm to farm, indirect movement type 15and Zone 4 boundary for enforcing control.

We similarly develop a reduced sized model for the number of farms infected MOE. We take the union of the relevant factors for cattle infected, and farms infected. This reduced the overall number of factors to be studied to 16. In addition to the 10 factors above, we also include: tracing effectiveness, Zone 2 boundary for enforcing control, surveillance visit frequency for detection, full resources available for depopulation, infectivity and probability of transmission applied to all markets and to all farms. We explain the implications of these factors on the outcome of the study in section

5 of this chapter. Description of factors has been retained from Axelsen (2012) and is attached as the Appendix for reference. We carry out a stepwise selection based on the BIC method to study the factors that are statistically significant. We present the statistics of the reduced model in Figure 22. The reduced model has an explanatory capacity of 84.9%. Thus, we conclude that the smaller saturated model with 16 factors is producing similar quality in the results as the saturated model with 47 factors which had an R^2 value of 85%. We are now able to condense the study from 47 factors to 16 factors without degrading the performance of the model. The sorted order of significance of each factor is depicted in Figure 23.

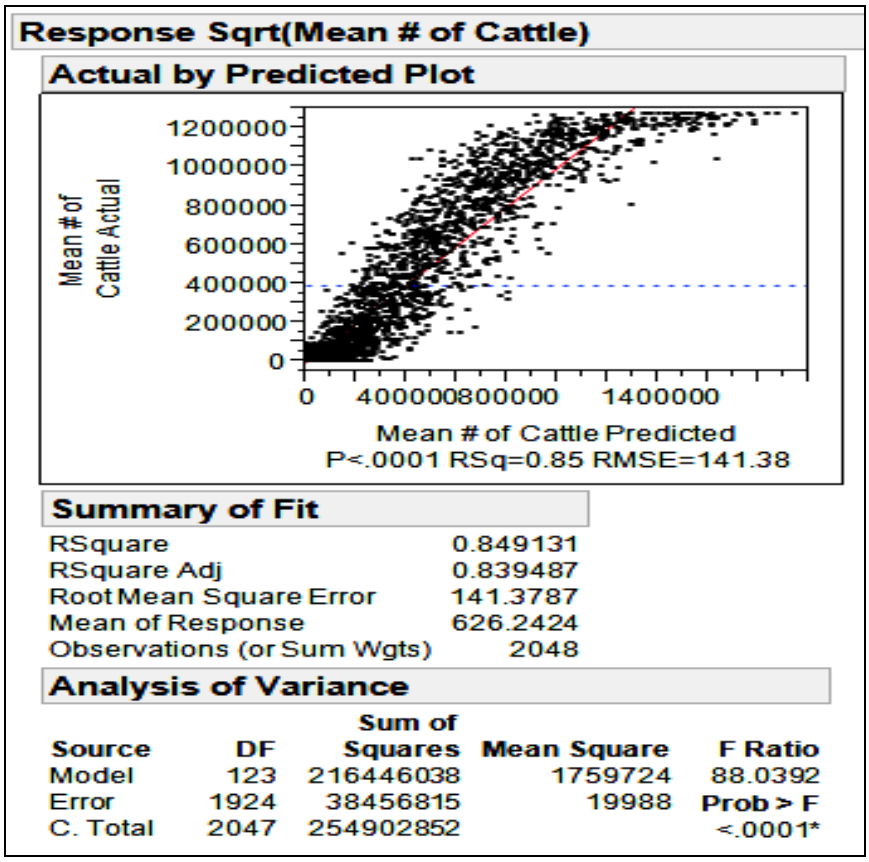
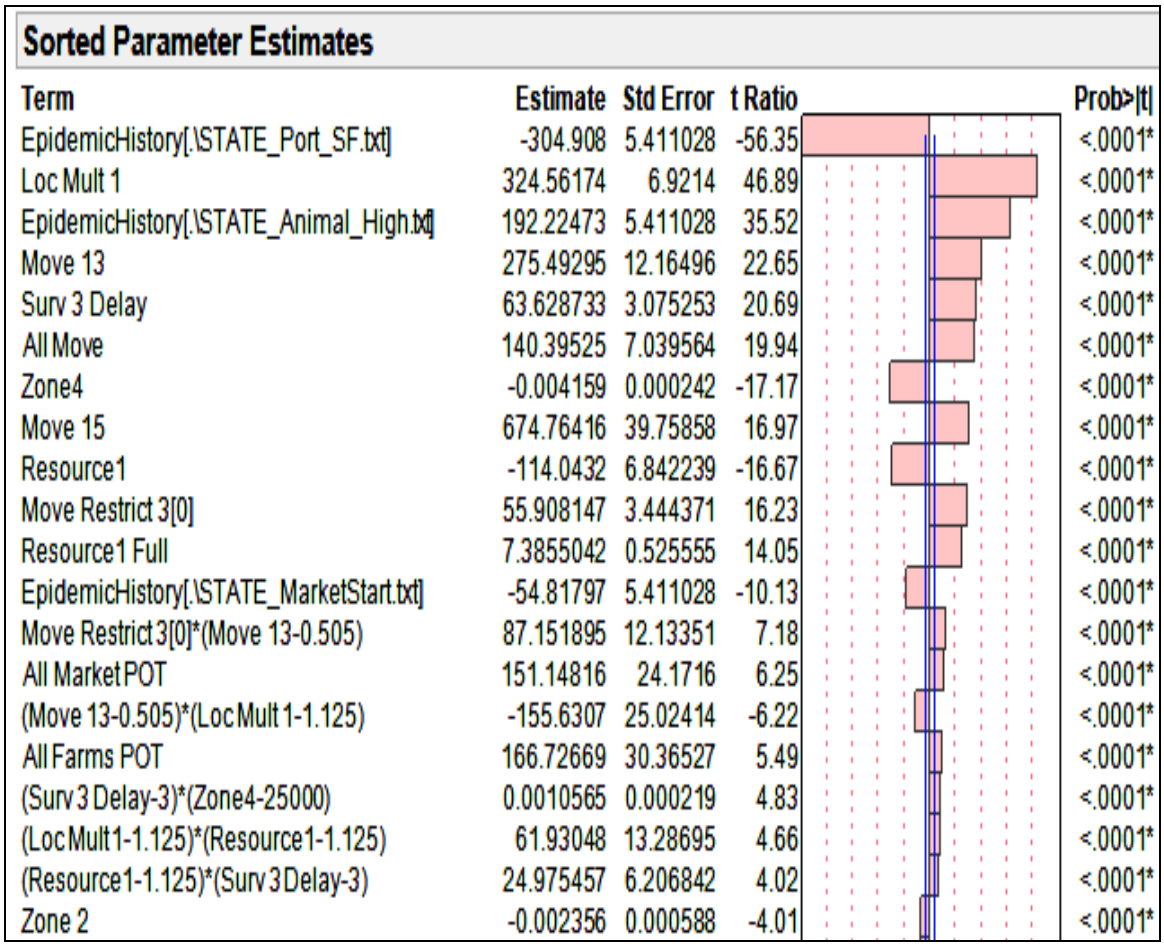


Figure 22. Graph highlighting the statistics of the reduced saturated model after the square root transformation. The saturated model includes interaction, quadratic, and cubic effects. We observe that even after reducing the model to 16 factors and including all interaction effects, quadratic and cubic effects, the R^2 value does not degrade beyond 85%. The analysis of variance p-value < 0.0001 shows that the model is approximately valid.



Sorted Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
EpidemicHistory[.\STATE_Port_SF.txt]	-304.908	5.411028	-56.35	<.0001*
Loc Mult 1	324.56174	6.9214	46.89	<.0001*
EpidemicHistory[.\STATE_Animal_High.txt]	192.22473	5.411028	35.52	<.0001*
Move 13	275.49295	12.16496	22.65	<.0001*
Surv 3 Delay	63.628733	3.075253	20.69	<.0001*
All Move	140.39525	7.039564	19.94	<.0001*
Zone4	-0.004159	0.000242	-17.17	<.0001*
Move 15	674.76416	39.75858	16.97	<.0001*
Resource1	-114.0432	6.842239	-16.67	<.0001*
Move Restrict 3[0]	55.908147	3.444371	16.23	<.0001*
Resource1 Full	7.3855042	0.525555	14.05	<.0001*
EpidemicHistory[.\STATE_MarketStart.txt]	-54.81797	5.411028	-10.13	<.0001*
Move Restrict 3[0]*(Move 13-0.505)	87.151895	12.13351	7.18	<.0001*
All Market POT	151.14816	24.1716	6.25	<.0001*
(Move 13-0.505)*(Loc Mult 1-1.125)	-155.6307	25.02414	-6.22	<.0001*
All Farms POT	166.72669	30.36527	5.49	<.0001*
(Surv 3 Delay-3)*(Zone4-25000)	0.0010565	0.000219	4.83	<.0001*
(Loc Mult 1-1.125)*(Resource1-1.125)	61.93048	13.28695	4.66	<.0001*
(Resource1-1.125)*(Surv 3 Delay-3)	24.975457	6.206842	4.02	<.0001*
Zone 2	-0.002356	0.000588	-4.01	<.0001*

Figure 23. The graph highlights the sorted order of significance with which a factor contributes towards the response variable for the reduced, 16 factor, saturated model. We see that epidemic history, local spread multiplier and market movement (movement type 13) are still the biggest contibutors of the disease in the reduced model.

b. Detection Time

This model is applicable to the detection time MOE. We follow similar stepwise BIC selection procedures for significant factors as we did for the mean number of cattle infected MOE. We get an R^2 value of 0.8695 with all the main effects, interaction and nonlinear quadratic and cubic effects. But we observed heteroscedasticity in the data, as was the case in the previous original model of mean number of cattle infected with the transformation as seen in Figure 24.

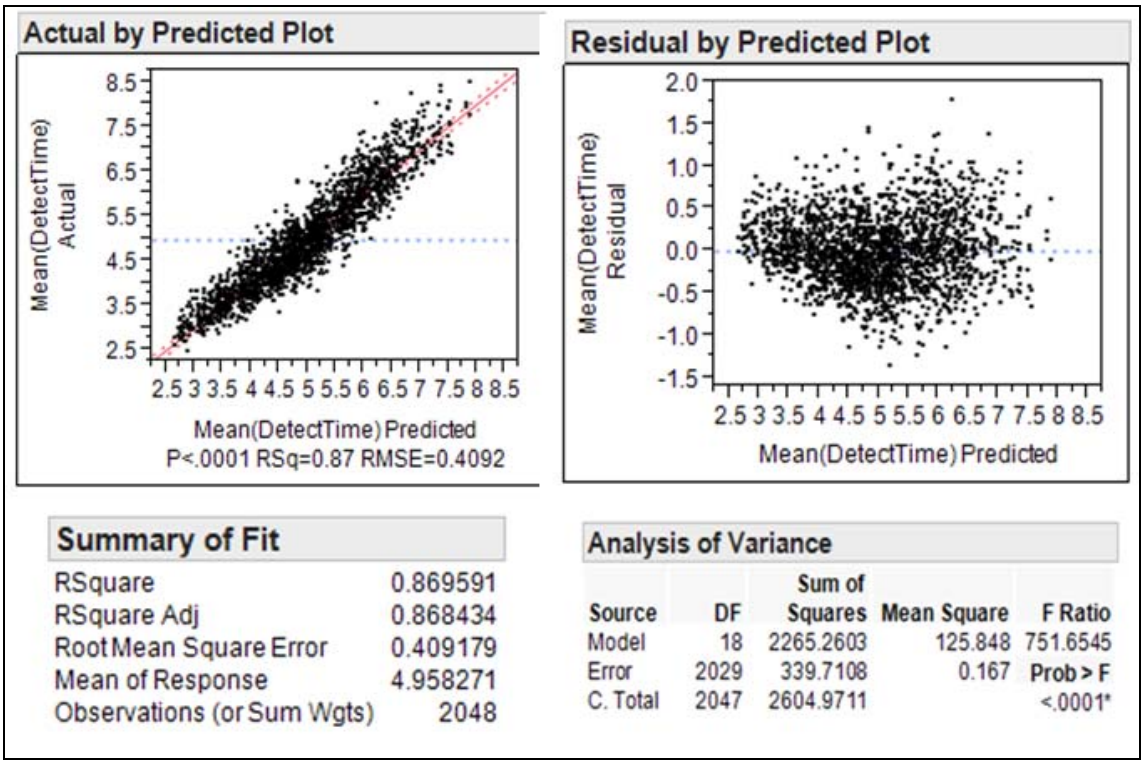


Figure 24. Graph highlighting the statistics of the reduced saturated model before the square root transformation for the detection time MOE. We observe that the reduced saturated model for detection time MOE includes all interaction, quadratic and cubic effects. The R^2 value is 0.869. The analysis of variance p-value < 0.0001 shows that the model is plausible. However, when we see the residual against fitted plot, we observe non-constant variance in the model.

With insights gained from the earlier model we did a square root Box-Cox transformation to resolve the problem of nonconstant variance. We fit the model again with square root of detection time and observe that the heteroscedasticity appeared to be removed from the model as seen in Figure 25. The statistics for the transformed detection time model is depicted in Figure 26.

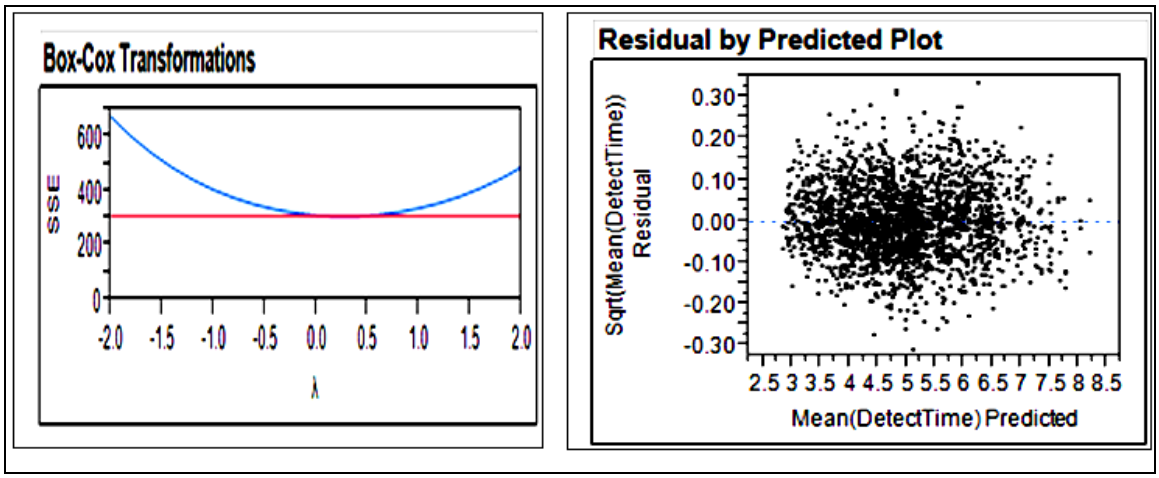


Figure 25. A graph showing requirement for Box-Cox transformation of the response variable , i.e., the detection time. We observe that the lambda value is between 0.4 and 0.5 indicating a requirement for a square root transformation. After the correction, the residual by predicted plot shows constant variance.

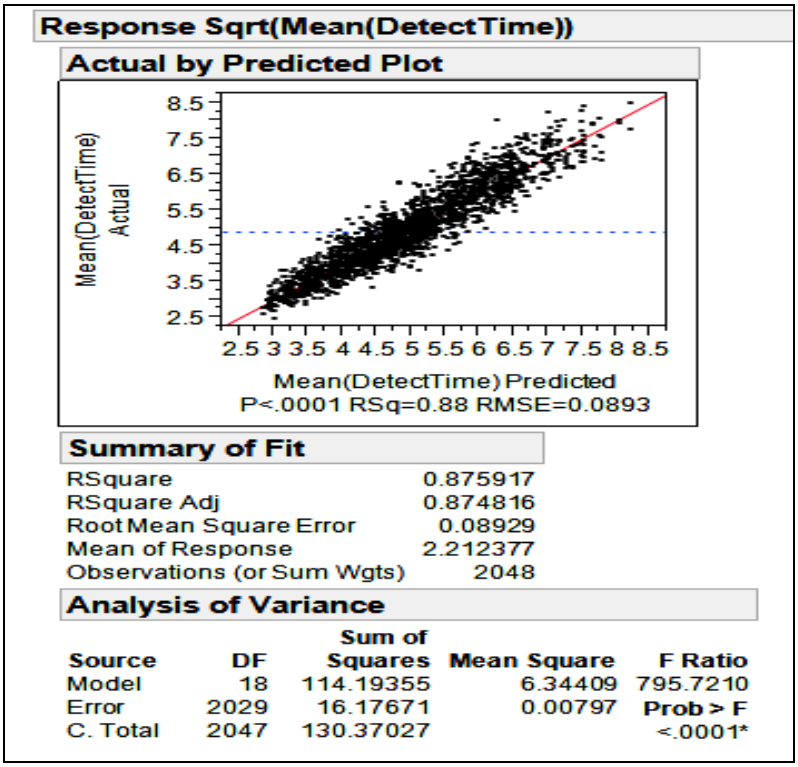


Figure 26. Graph highlighting the statistics of the reduced saturated model after the square root transformation for the detection time MOE. We observe that the reduced saturated model for dtection time MOE with all interaction effects, quadratic and cubic effects has an R^2 value is 0.8759. The analysis of variance p value < 0.0001 shows that the model is plausible.

We observe that main, interaction and nonlinear effects as highlighted in Figure 27 are significant at $\alpha = 0.05$. Surveillance is highest in the list of sorted factors, highlighting its contribution towards the control of the disease. We observe that for the detection time MOE only about five to six factors, with t-ratio value more than 10, are contributing towards the explanatory power of the model, as shown in Figure 27. This indicates that even a smaller metamodel may work for this MOE as only a few factors have a high t-ratio. We use a partition tree in section D of this Chapter to quantify the contribution of the factors towards the overall explanatory power of the model. The major contributors for the detection time response are surveillance, epidemic history, local spread, market movement and the quadratic effect of infectivity. We carry out sensitivity analysis for the significant contributors and highlight their effects in section C (4) of this chapter.

Sorted Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Surveillance3.DelayToDetection.GeneralSurv_Dairy_before	0.1502098	0.00172	87.34	<.0001*
EpidemicHistory.StateFileName{.\STATE_Premise_High.txt&.\STATE_Animal_High.txt-.\STATE_Port_SF.txt&.\STATE_MarketStart.txt}	-0.138133	0.001952	-70.77	<.0001*
LocalSpread1.Multiplier	-0.086215	0.003898	-22.12	<.0001*
MovementType13.NumberPerTimePeriod.24.31.32.33.34.41.43.51.53.61.63.73.211.213.214.	-0.094563	0.006921	-13.66	<.0001*
(Infectivity1.TimeToClinicalSigns-4.5)*(Infectivity1.TimeToClinicalSigns-4.5)	0.0068076	0.000541	12.58	<.0001*
Surveillance3.VisitFrequency.GeneralSurv_Dairy_before	0.0321466	0.00272	11.82	<.0001*
AllMovements.MovementDistance	-0.036583	0.003878	-9.43	<.0001*
MovementType15.NumberPerTimePeriod.24.34.114.214.314.310.211.213.51.61.53.63.121.131.151.161.	-0.193729	0.022601	-8.57	<.0001*
(Infectivity1.TimeToClinicalSigns-4.5)*(Infectivity1.TimeToClinicalSigns-4.5)*(Infectivity1.TimeToClinicalSigns-4.5)	-0.002297	0.000307	-7.49	<.0001*
AllMarkets.ProbabilityOfTransmission	-0.071442	0.01367	-5.23	<.0001*
Surveillance1.DelayToDetection.GenSurv	0.0051338	0.001371	3.75	0.0002*
LocalSpread1.RelativeSusceptibility.sheep.	-0.050781	0.013899	-3.65	0.0003*
(MovementType13.NumberPerTimePeriod.24.31.32.33.34.41.43.51.53.61.63.73.211.213.214.-0.505)*(AllMovements.MovementDistance-1.125)	-0.04489	0.013709	-3.27	0.0011*
(AllMovements.MovementDistance-1.125)*(AllMovements.MovementDistance-1.125)	0.0273964	0.008759	3.13	0.0018*
(Surveillance1.DelayToDetection.GenSurv-4.5)*(Surveillance3.DelayToDetection.GeneralSurv_Dairy_before-3)	0.0035947	0.001175	3.06	0.0022*
(MovementType13.NumberPerTimePeriod.24.31.32.33.34.41.43.51.53.61.63.73.211.213.214.-0.505)*(LocalSpread1.Multiplier-1.125)	0.0422235	0.013921	3.03	0.0025*
(AllMovements.MovementDistance-1.125)*(Surveillance3.VisitFrequency.GeneralSurv_Dairy_before-1.75)	-0.015936	0.005641	-2.82	0.0048*
(MovementType14.NumberPerTimePeriod.41.-0.028)*(AllMarkets.ProbabilityOfTransmission-0.75)	-3.747526	1.367689	-2.74	0.0062*
Infectivity1.TimeToClinicalSigns	0.0059823	0.002452	2.44	0.0148*
(LocalSpread1.Multiplier-1.125)*(Surveillance3.DelayToDetection.GeneralSurv_Dairy_before-3)	-0.007372	0.003429	-2.15	0.0317*

Figure 27. Factors that are significant in a reduced regression model, using the same 16 factors as Figure 23, at $\alpha = 0.05$. Tests involving additional factors, on top of these 16, did not produce a better explanatory power. We observe that in addition to main effects, several interaction effects and nonlinear effects are significant at $\alpha = 0.05$.

4. Sensitivity Analysis based on MOEs

Figure 28 describes the sensitivity of the response variable to varying values of the independent variables. The figure includes a sensitivity index in the form of a triangle. Higher sensitivity to the factor results in a larger triangle. Triangle with apex up indicates that the value of the chosen MOE would increase as the value of the factor is increased from low to high and vice versa. Sensitivity is essentially the slope of the line of the response variable vs. the independent variable. We present the analysis for two MOEs that are not strongly correlated: the number of cattle infected and the detection time.

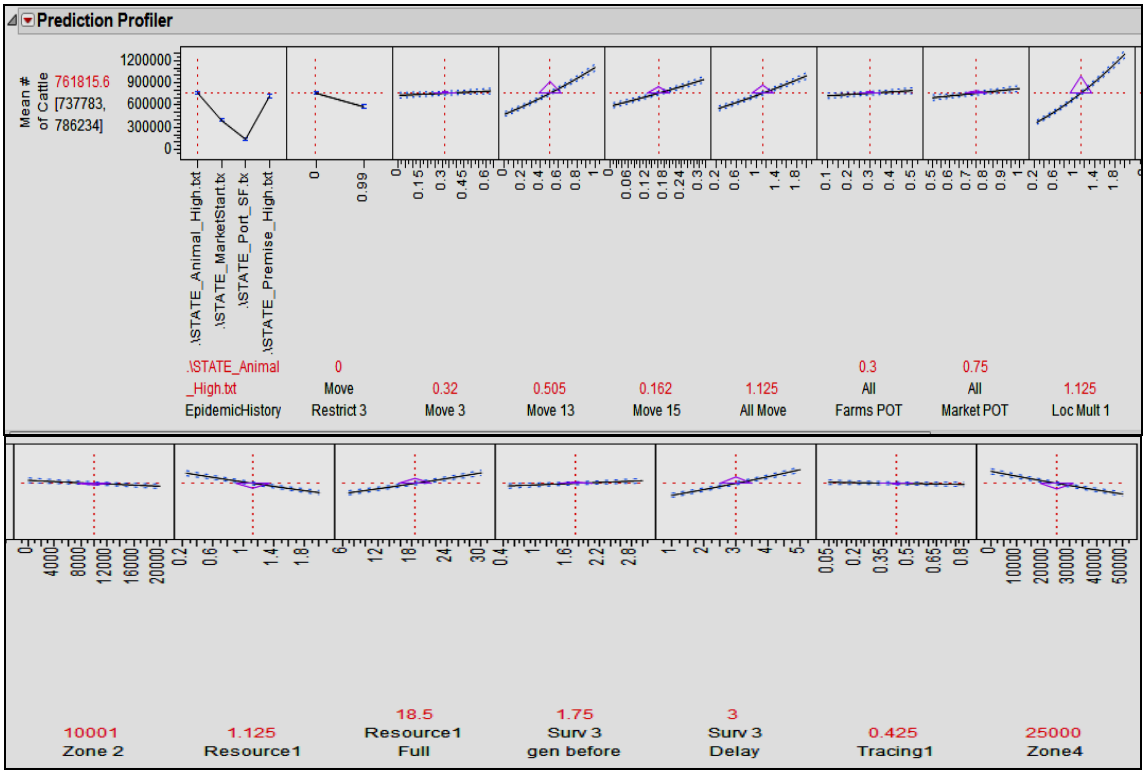


Figure 28. A sensitivity graph for the response of the mean number of cattle infected. We include the sensitivity index in the graph. The area of the triangle is proportional to the sensitivity of the factor. A triangle with apex up has a positive slope and a triangle with downward slope has a negative slope.

We use the worst case initial condition, high animal density, to carry out the analysis. Sensitivity analysis is based on extreme values of the independent factors. For instance, we can never practically ensure zero market movement or 100% market movement. Practically, the probability of market movement will be between zero and one. But for sensitivity analysis purposes, we use extreme values for the factors. The number of infected cattle MOE is most sensitive to the following factors that may be targeted to reduce the spread of the disease:

- *Movement Restriction*: Movement restriction is a binary variable indicating whether the movement restriction is enforced on all the markets in Zone 3 or only in control and surveillance zones. This factor has a negative slope indicating that as the movement restriction increases the mean number of cattle getting infected with the virus significantly decreases. Comparing extreme values of the market movement restriction parameter, the number of cattle infected is reduced by 25%.

- *Market Movement*: Market movement type 13 has a large sensitivity index as can be seen from the size of the triangle in Figure 28. This factor is relevant for all types of livestock. In addition to the main effect, several interaction effects, quadratic and cubic effects of this factor are observed to be statistically significant. When we vary the probability of movement from 0 to 1, we see a 1.25 fold increase in the number of cattle infected. This factor however did not have such a large impact on the detection time. Figure 29 depicts a scatter plot of the market movement parameter vs. the number of cattle infected, grouped by initial condition. We observe that more cattle are infected if the infection starts in a high animal or high premise dense farm. The start of infection in the market has a bigger spread than at the San Francisco port.

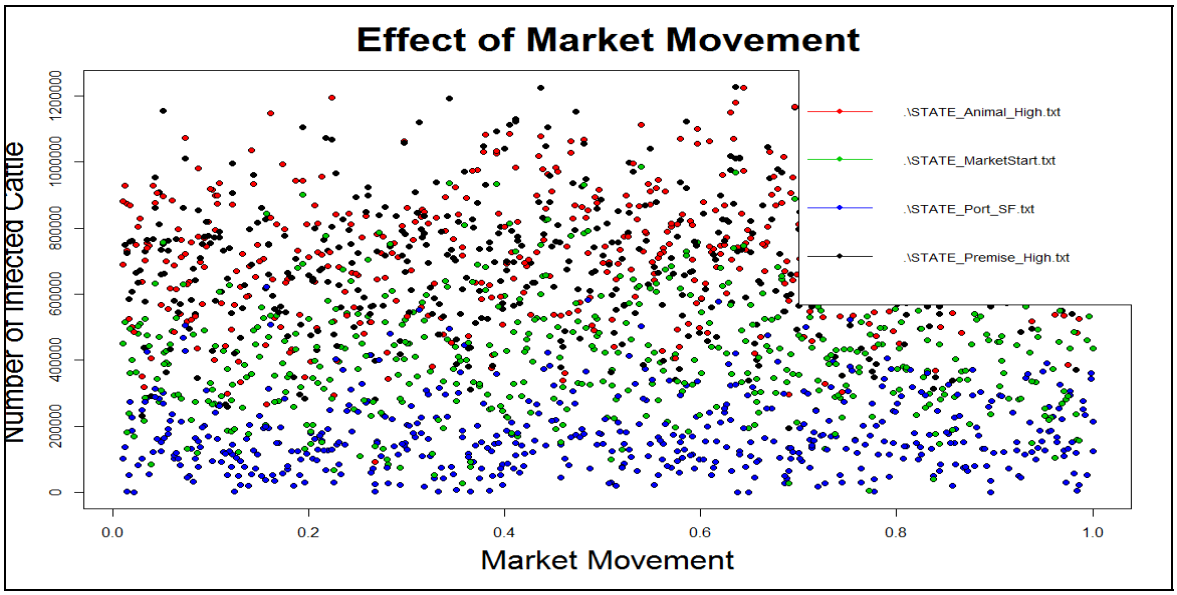


Figure 29. Mean number of infected cattle plotted against the market movement grouped by their epidemic history. We observe that more cattle are infected if the origin of infection is a high animal dense farm or from a high premise dense area.

- *Local Spread Multiplier*: The local spread multiplier has the largest sensitivity index in our model indicated by the largest size of the triangle with the apex up as compared to other factors. This is expected as local spread is one of the most common causes of transmission of the virus at close distances. During the 2001 U.K. FMD outbreak, the source of infection of 1,802 out of 2,030 infected premises was attributed to local spread (Stevenson, 2007). When we vary the local spread multiplier between 0.2 and 2, we see that there is a 4.5 times increase in the number of cattle infected. We also observe interaction, quadratic and cubic effects of local spread to be significant in the model. This factor has the biggest potential of turning the disease into an epidemic as seen by the 4.5 times increase between the high and the low value of the sensitivity index. Figure 30 depicts a scatter plot of the local spread parameter vs. the number of cattle infected, grouped by initial condition.

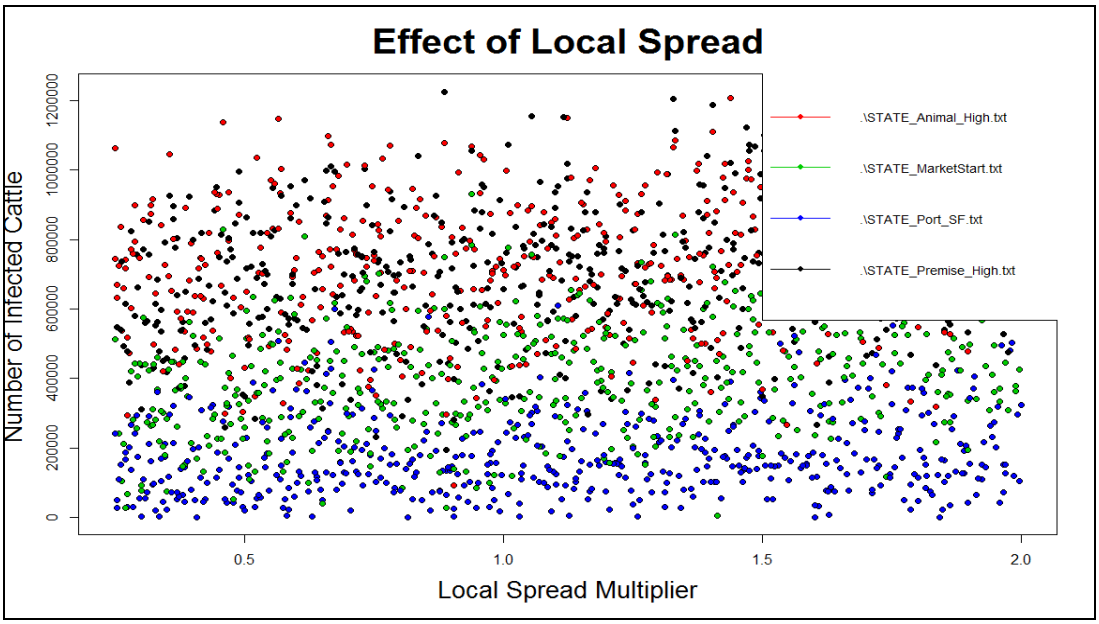


Figure 30. Mean number of infected cattle plotted against the local spread multiplier grouped by their epidemic history. We observe that more cattle are infected if the origin of infection is a high animal dense farm or from a high premise dense area.

- *Surveillance*: Surveillance measures at dairy-like facilities are highly significant in controlling the spread of FMDV. Smaller time periods between visits at the farms placed in surveillance zones result in smaller detection delays and consequently a smaller mean number of infected cattle. There are seven surveillance factors in the DOE, but only dairy-like surveillance shows as significant because there are much more cattle in Zone 3 as compared to other livestock. We also observe high interactions between surveillance measures and other control options such as tracing, as indicated by the significant interaction effects. Increasing the dairy-like surveillance delay from one to five days increases the number of cattle infected by approximately 42%.

- *Resource Utilization*: Initially, in the simulation control measures, only 2,000 animals per day can be depopulated. The full resource capability of depopulating 20,000 animals per day is not available until a certain time after detection. Changing this parameter from 7 to 21 days results in an increase of 20% in the number of cattle infected.

- *Tracing*: Tracing delay caused due to forgetfulness or due to unavailability of resources increased the mean number of infected cattle by 20%. We assume that manual tracing is required. This control factor cannot be studied in isolation as we observed statistically significant interaction effects between tracing and surveillance, as well as tracing and control measures in Zone 4.

- *Zonal Boundary*: We observe that the MOEs in Zone 3 are more sensitive to the control measures in Zone 4 as compared to Zone 2. This may be attributable to the fact that a larger area is being surveilled or controlled in Zone 4. Also, there could be more intra-zonal market movement between Zone 3 and Zone 4. However, control measures in both adjoining zones had statistically significant impact on the MOEs. This factor also had interactions with other control measures applied in Zone 3.

For the MOE of detection time, surveillance delay is the only parameter, other than epidemic history, with high sensitivity, as can be seen in Figure 31. Greater delay in enforcing dairy-like surveillance results in bigger detection times. We observe a 75% increase in the detection time if surveillance delay was five days as compared to one day.

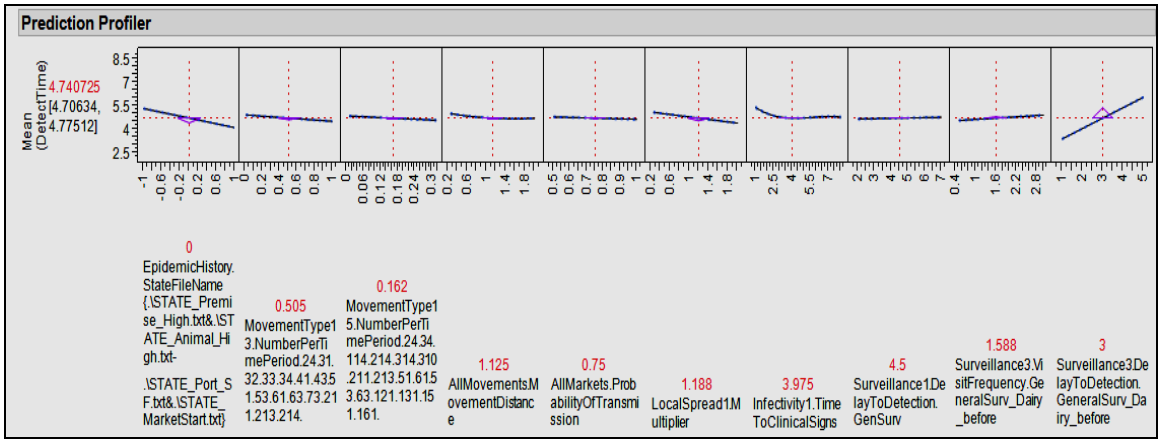


Figure 31. The sensitivity graph for the detection time MOE. We observe that only two factors have a large sensitivity index (surveillance delay and the epidemic history), as indicated by the slope of the lines.

D. PARTITION TREE ANALYSIS

We use a partition tree to further our analysis and gain useful insights. A partition tree is an analytical tool that iteratively splits the data to maximize the difference in the mean of the response variables of two distinct groups of the predictor variable. Each split uses the independent variable and split threshold that gives the greatest difference in means for the response variable (SAS, 2010).

1. Partition Tree Model for Detection Time

For the regression model with the detection time as the response variable, we had identified dairy-like surveillance to be the most significant contributor towards reducing the detection time. We expected to see the split first to occur for this factor in the model. We ran the partition trees for the detection time MOE and, as expected, the first split is placed at the surveillance delay of 3.2857 days, as seen in Figure 32. This means that if the surveillance delay is less than 3.2857 days, we expect to detect the infection in an average of 4.36 days. On the other hand, if surveillance delay is greater than 3.2857 days, then detection time increases to an average of 5.75 days, a 32% increase.

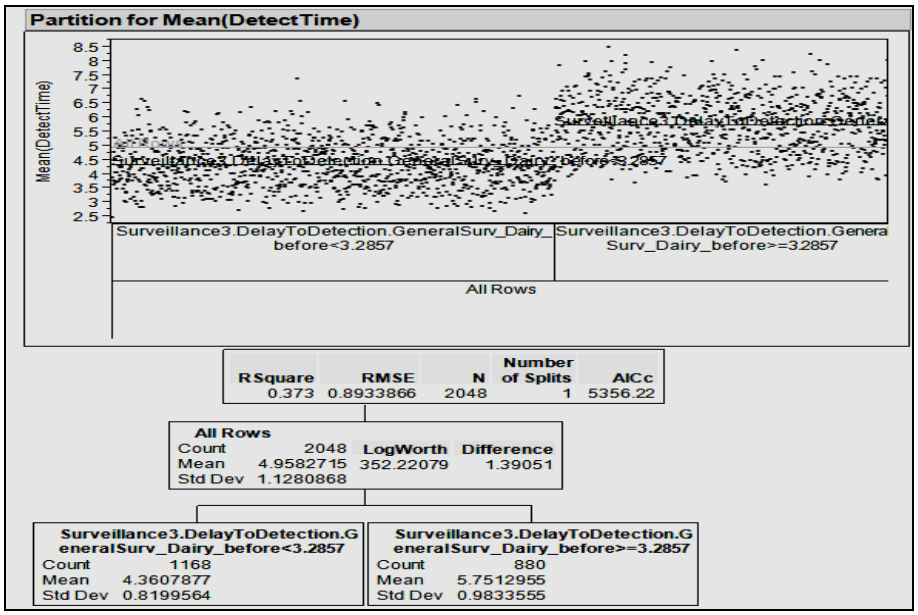


Figure 32. Statistics of the partition tree model for the detection time MOE. We observe that the first split occurs for the dairy-like surveillance parameter indicating that surveillance has the biggest impact on the detction time.

The next split occurs for the type of epidemic history. If the initial trigger of the infection was in high animal or high premise dense locations, then the mean detection time was 5.04 days and if it was in a market or in the San Francisco port then the mean detection time was 6.46 days. We do 15 splits to achieve a R^2 value of .815 and observe that only five factors contribute to the splits, as shown in Figure 33. The most significant effect in the partition tree model was due to surveillance delay. The partition tree model further validates our observation that a smaller metamodel with only five factors may be sufficient to explain most of the variability in the system.

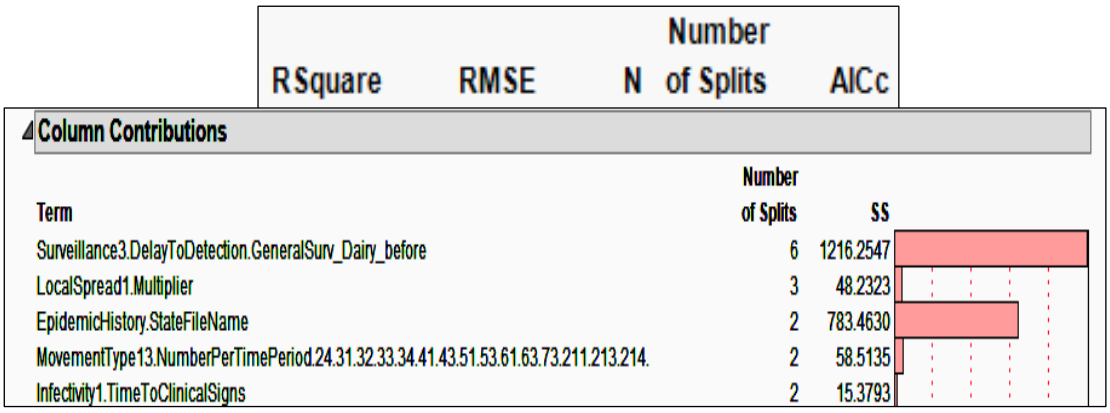


Figure 33. Factor contributions in terms of explanatory power in a partition tree model for the detection time MOE. We observe that six out of 15 splits occur due to dairy-like surveillance, indicating its significance in the partition tree model.

2. Partition Tree Model for Mean Number of Cattle Infected

In our regression model for the mean number of cattle infected we observe that the epidemic history, local spread multiplier, market movement and surveillance delay are the most significant contributors for the spread of the disease based on the sensitivity index (see Figure 28). We expected to see these factors also contributing in the partition tree model.

We run the partition tree model for this MOE and observe that the first split occurs for epidemic history followed by the local spread multiplier as shown in Figure 34.

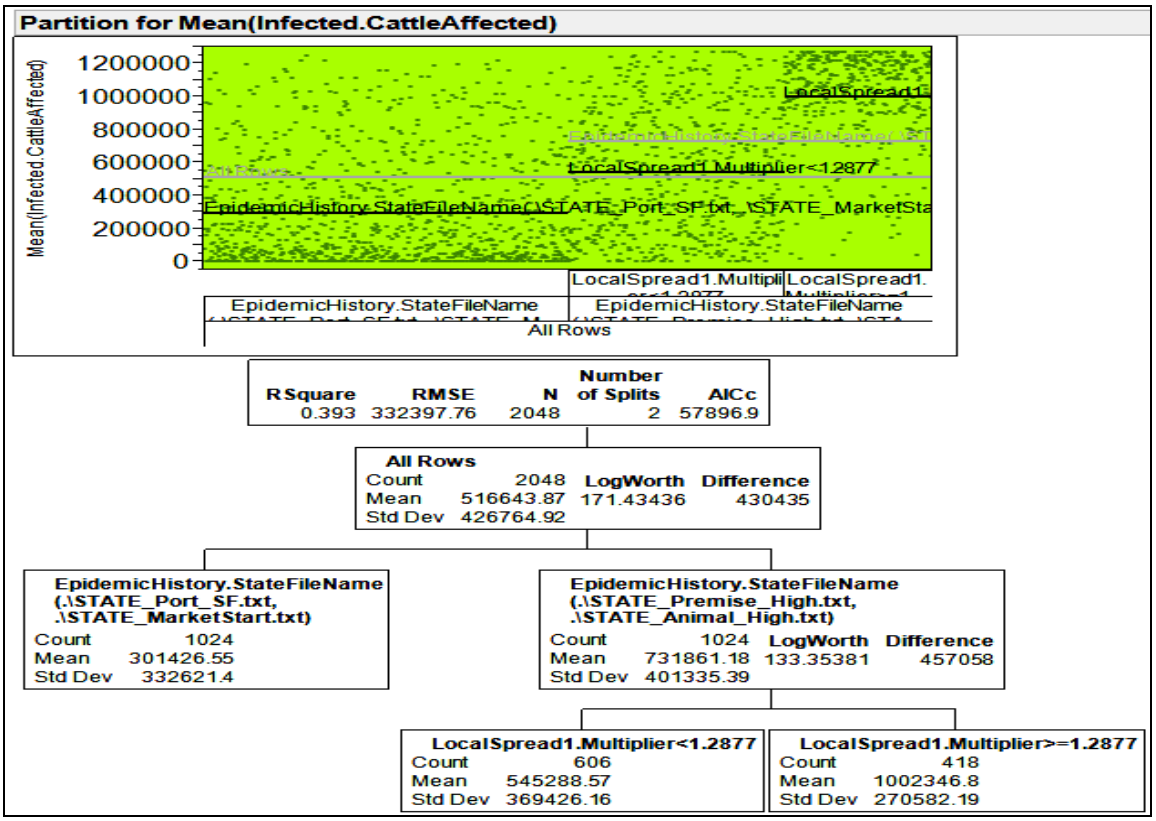


Figure 34. Statistics of the partition tree model for the number of cattle infected. We observe that the first split occurs for epidemic history, followed by local spread.

We observe that epidemic history has the highest impact on the mean number of cattle infected. If the origin is market or the San Francisco port, then the average number of infected cattle is approximately 301,426, whereas if the origin of infection is in an animal or premise dense location, then the average number of cattle infected is 731,861. The next split occurs due to the local spread multiplier at a value of 1.2877, indicating that the average number of cattle infected will be approximately 1.42 times less when the local spread is restricted to 4,000m as compared to when the spread goes beyond 4,000m. We carry out 15 splits to get a R^2 value of 0.681. All the significant factors are shown at Figure 35.

RSquare	RMSE	N	Number of Splits	AICc
0.681	240901.59	2048	15	56604.5

Column Contributions

Term	Number of Splits	SS
LocalSpread1.Multiplier	5	9.2244e+13
Surveillance3.DelayToDetection.GeneralSurv_Dairy_before	3	1.8539e+13
EpidemicHistory.StateFileName	2	1.1876e+14
MovementType13.NumberPerTimePeriod.24.31.32.33.34.41.43.51.53.61.63.73.211.213.214.	2	1.4218e+13
AllMovements.MovementDistance	1	3.9219e+12
Zone4.OutsideRadius1.SurvZone	1	5.2676e+11
Resource1.PerTimePeriod	1	5.7562e+12

Figure 35. Factor contributions for the number of cattle infected. We observe that five out of 15 times, the split occurrs at local spread.

We gather following information from the partition tree model of infected cattle:

- Initial infection at a market place has a greater impact than infection originating at the San Francisco port.
- If the surveillance delay can be kept below 2 days than the average number of infected cattle can be reduced by half as compared to a surveillance delay of more than 2 days.
- If the overall market movement of all livestocks is kept under 45% as compared to no market movement restriction, then the number of cattle infected can be reduced by 25%.

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V. CONCLUSIONS

We divide this Chapter in three subsections. In the first section, we summarize the critical insights that we gain from our analysis. In section two, we discuss the main differences that we observe in a regional model of Zone 3 against the full model for entire California (Axelsen, 2012). Finally, we submit our recommendation for future work.

A. CRITICAL INSIGHTS GAINED

The main results of our analysis of FMD spread are as follows:

- *Initial Condition*: Initial condition of the disease plays a significant role in the spread of the disease. We consider four starting scenarios: high animal density region, high premise density region, market, and port of San Francisco. Among the scenarios, the disease spread is almost twice as high when the infection originates in high animal or high premise dense areas. However, the detection time is 28% shorter if the initial infection originates in high premise or high animal dense areas. The impact of initial starting condition on the mean number of cattle infected is depicted in Figure 36.

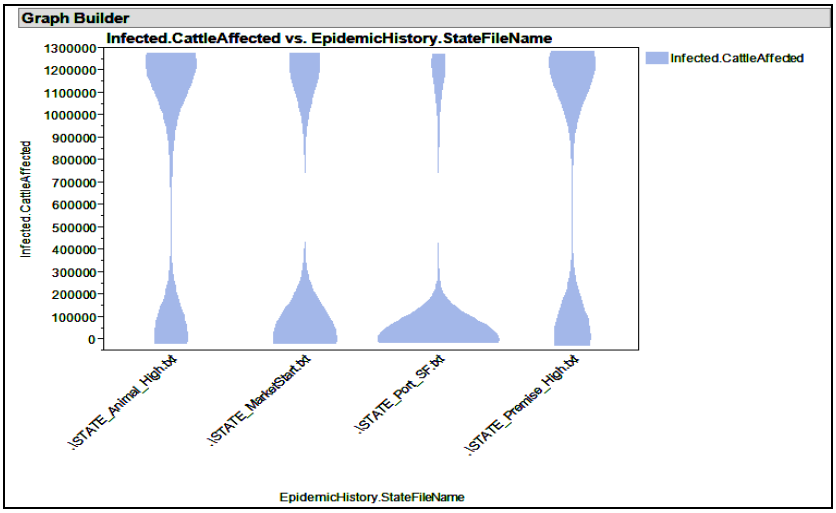

Figure 36. Spread of FMDV in cattle based on the starting scenario. We observe that infections originating from high animal and premise dense farms, and from market are significant contributors.

Local Spread: The local spread parameter captures the proximity-based spread of FMD between premises. Out of all disease and control factors, epidemic progression has the highest sensitivity to local spread. Interaction and non-linear effects are significant for this parameter. Restricting local spread to less than 4,000m results in a 1.42 fold reduction in the mean number of cattle infected; however, the extent to which we can restrict local spread in a real-world scenario is unknown.

- *Market Movement*: Market movement of cattle is a major contributor towards the spread of the disease. Interaction and non-linear effects for market movement are significant for this parameter. Our experimental results indicate that if a typical premise sends an animal to market every 2.2 days instead of every day, we will see a 25% reduction in the mean number of cattle infected.

- *Surveillance*: Surveillance measures at dairy-like facilities are highly significant. We observe high interactions between surveillance and other control measures such as tracing and depopulation. Among the control measures, surveillance has the maximum impact towards reducing the spread of the disease. If there is less than a three day delay in between suspecting an FMD outbreak and declaring an FMD outbreak at dairy-like facilities, we see a reduction in mean detection time for a new epidemic of 32%. A delay of less than two days in the same parameter reduces the average number of infected cattle by half.

Our models show significant interaction effects between the most effective control measures—market movement, and surveillance—and other control measures such as tracing, vaccination and depopulation. In addition, our model suggests that restricting local spread and controlling direct, indirect and market movements can be decisive towards controlling the spread of the disease in California. Furthermore, surveillance measures and movement control in adjoining zones, in addition to the primary outbreak zone, may help in reducing disease spread.

B. COMPARISON OF ZONAL MODEL WITH THE STATE MODEL

One of the major aims of the thesis was to determine if a regional model can establish more detailed relationships between the response MOEs and the factors contributing to the spread of FMD by incorporating the recommendations from Axelsen (2012). We observe that the zonal model differs from the state model in terms of parameter settings and the output from the simulation runs as enumerated below.

1. Parameter Settings and Modeling Approach

In addition to selecting only the statistically significant factors from Axelsen (2012) and reducing the size of our base model to 47 factors from 73 factors, we made the following changes to the structure of the model:

- *Market Movement*: Due to the huge dimension of the problem both in number and space, market movement could not be studied in adequate detail for the state model. However, for the zonal model, we introduce a factor for market movement and study its effect on the response MOEs in greater detail.

- *Local Spread*: For the zonal model, we study the effect of reducing the local spread distance to 5,000m against 6,000m in the state model. This reduces the run time for the replications without degrading the explanatory capacity of the model.

- *Sensitivity Analysis*: For the zonal model we carry out sensitivity analysis for all the 16 factors quantitatively. The same could not be achieved for the state model, probably due to higher number of factors.

2. Comparison of Statistical Outputs

We observe the following differences between the zonal and the state model that stem out from our analysis:

- *Explanation of Variance*: The state regression model with 72 factors explains 40% of the variability in the data with an R^2 value of 0.40,

whereas the zonal reduced saturated regression model with 16 factors explains 85% of the variability in the model.

- *Explanation of Interaction and Non*-linear Effects: Using metamodeling techniques, we reduce the scope of the zonal study to only 16 factors. This facilitates study of interaction and non-linear effects of each factor in greater detail.

- *Boundary for Control Area and Surveillance Zone*: Axelsen (2012) highlights that sizes of the control area and surveillance zones were not significant in the state model. However, for the zonal model, both Zone 4 boundary and Zone 2 boundary are significant in controlling the spread of the disease in Zone 3. Intra-zonal movement between farms and markets may have interaction effects on control measures in Zone 3. Also Zone 4 has a higher sensitivity index in comparison to Zone 2. We will require better local knowledge of farms and markets and intra-zonal movements to do any causative analysis. We conclude that 10km is a good starting point for controlling the disease initially. But as the days to detection increase, interactions between the zonal boundary, local spread and surveillance measures indicate that increasing the radius of both control areas and surveillance zones (not only for the zone under study but also for adjoining zones) may reduce the number of animals infected considerably.

- *Depopulation*. For the state partition tree model, the size and availability of depopulation resources is one of the largest contributory factors for controlling the spread of FMD. Axelsen (2012) states "this is surprising as our model does not use preemptive depopulation" and suggests sensitivity analysis to be conducted for depopulation measures. For the zonal model, depopulation resources though significant, appear much later in the hierarchy of control measures (refer to Table 6).

C. RECOMMENDATIONS FOR FUTURE RESEARCH

Our model could not capture a few of the important aspects of the spread of FMDV essentially due to a lack of data available on the subject or due to incompatibility with ISP. We highlight those aspects as future research work in this field.

- *Airborne Spread*: We could not parameterize airborne spread in our model. Under favorable conditions the aerosolized virus can cover distances beyond the local spread distance and may need separate parameterization. We used a distance multiplier to achieve this as a surrogate to the airborne spread. We observed that the distance multiplier was significant for all the MOEs. Accurate data for the parameterization of airborne spread can produce better results in this field.

- *Infectivity*: Nonlinear terms of infectivity are significant for the detection time both in the regression model as well as in the partition tree. However, the main effect of infectivity is observed to be very low in the prioritized significance list as seen in Figure 27. We expect that the probability to infect a particular farm increases the detection time decreases. The same was not seen in the model as we observed that after about 3.1 days of infection the detection time becomes almost constant. The first split occurs at 3.1 days from infectivity in the partition model. This factor may need further research.

- *Large Scale Epidemic*: A large scale epidemic is not an MOE in the model as we understand that there is no fixed criterion for defining an epidemic. We use the MOE of number of cattle infected as a surrogate to understand the scale of the outbreak. Future work in consultation with subject matter experts may provide a better tool for quantifying when the outbreak may be classified as an epidemic.

In addition, the following may be undertaken to improve the model and analysis for the spread of FMD in California. Market movement is observed to be a significant contributor towards the spread of FMD in the zonal model. Based on the parameter settings, it is recommended that this factor may be introduced in the state model and its interaction with all the 72 factors from Axelsen (2012) may be studied in greater detail.

Significant interactions with market movement other than those observed in the zonal model may need further elucidation. Additionally, future work may apply the principal of robust design that uses loss functions to minimize the effect of causes of variation without eliminating any of the factors (Shyam, 2002). Robust design will reduce the sensitivity of the model towards factors that cannot be controlled such as airborne spread, infectivity, and local spread.

APPENDIX. DESCRIPTION OF THE DESIGN OF EXPERIMENT

Factor name	Low Level	High Level	Factor Description
MovementType1:NumberPerTimePeriod[114|214|314|24|34]	**0.01**	**0.14**	**Movement_Farm_Farm_Backyard:** Direct Contact movement rate from backyard premises (All Species). **Poisson** Distribution with means varied between low and high levels. Types affected: 114|214|314|24|34
MovementType2:NumberPerTimePeriod[310]	**0.01**	**0.56**	**Movement_Farm_Farm_Goat:** Direct Contact movement rate from Goat premises. **Poisson** Distribution with means varied between low and high levels. Types affected: 310
MovementType3:NumberPerTimePeriod[211|213]	**0.01**	**0.6300**	**Movement_Farm_Farm_Sheep:** Direct Contact movement rate from Sheep premises. **Poisson** Distribution with means varied between low and high levels. Types affected: 211|213
MovementType7:NumberPerTimePeriod[33]	**0.4000**	**0.7000**	**Movement_Farm_Farm_DairyL:** Direct Contact movement rate from Large Dairy premises. **Poisson** Distribution with means varied between low and high levels. Types affected: 33
MovementType8:NumberPerTimePeriod[41]	**0.01**	**0.0370**	**Movement_Farm_Farm_Calf_HeiferS:** Direct Contact movement rate from Small Calf/Heifer premises. **Poisson** Distribution with means varied between low and high levels. Types affected: 41

MovementType9:NumberPerTimePeriod[43|73]	**0.01**	**1.96**	**Movement_Farm_Farm_Calf_HeiferL:** Direct Contact movement rate from Large Calf/Heifer premises. **Poisson** Distribution with means varied between low and high levels. Types affected: 43|73
MovementType13:NumberPerTimePeriod[24|31|32|33|34|41|43|51|53|61|63|73|211|213|214]	**0.01**	**1**	**Movement_farm-market:** Market movement with probability of transmission constant = 0.8. **Poisson** Distribution with means varied between low and high levels. Types affected (All types of animals in Zone 3): 24|31|32|33|34|41|43|51|53|61|63|73|211|213|214
MovementType14:NumberPerTimePeriod[41]	**0.01**	**0.046**	**IDMovement_Size1:** Indirect Contact movement rate for Small Calf/Heifer premises. Poisson Distribution with means varied between low and high levels. Types affected: 41
MovementType15:NumberPerTimePeriod[24|34|114|214|314|310|211|213|51|61|53|63|121|131|151|161]	**0.01**	**0.314**	**IDMovement_Size2:** Indirect Contact movement rate for a group of premise types that have the same order of magnitude mean rate. Poisson Distribution with means varied between low and high levels. Types affected: 24|34|114|214|314|310|211|213|51|61|53|63|121|131|151|161
MovementType16:NumberPerTimePeriod[153|163]	**0.01**	**1.63**	**IDMovement_Size3:** Indirect Contact movement rate for a group of premise types that have the same order of magnitude mean rate.

			Poisson Distribution with means varied between low and high levels. Types affected: 153|163
MovementType17:NumberPerTimePeriod[31|32|43|73]	**0.01**	**2.0340**	**IDMovement_Size4:** Indirect Contact movement rate for a group of premise types that have the same order of magnitude mean rate. Poisson Distribution with means varied between low and high levels. Types affected: 31|32|43|73
MovementType18:NumberPerTimePeriod[33]	**0.862**	**1.0413**	**IDMovement_Size5:** Indirect Contact movement rate for Large Dairy premises. Poisson Distribution with means varied between low and high levels. Types affected: 33
AllMovements:MovementDistance	**0.25**	**2**	A multiplier applied to the distance bands for all movement types simultaneously.
AllFarms:ProbabilityOfTransmission	**0.1**	**0.5**	The constant to be used as the basis to calculate the probability of transmission for all farm to farm movements (Direct and Indirect). This number is an input to functions to calculate the probability of transmission for different species.
AllMarkets:ProbabilityOfTransmission	**0.5**	**1**	The constant to be used as the basis to calculate the probability of transmission for all farm to market and market to farm movements.
LocalSpread1:Multiplier	**0.25**	**1.5**	A multiplier applied to the distance bands for local spread. .

LocalSpread1:RelativeSusceptibility[swine]	**0.001**	**0.1**	Suceptability of swine to local spread relative to cattle.
LocalSpread1:RelativeSusceptibility[sheep]	**0.005**	**0.5**	Suceptability of sheep to local spread relative to cattle.
Infectivity1:TimeToClinicalSigns	**1**	**8**	The Beta value of a LogLogistic Curve with parameters (2, Beta, 4.1436) describing the time until clinical signs are evident on the premise.
Zone2:OutsideRadius1:ControlArea	**1**	**20000**	**Control Measure:** Outside radius of the control area in meters.
Zone3:OutsideRadius1:VaccZone	**0**	**20000**	**Control Measure:** Outside radius of the vaccination zone in meters.
Zone4:OutsideRadius1:SurvZone	**0**	**50000**	**Control Measure:** Outside radius of the Surveillance zone in meters.
Resource1:PerTimePeriod	**0.5**	**2**	**DepopResource:** a multiplier applied to the number of animals able to be culled in a day. When multiplier = 1, the animals culled per day (regardless of species) = 20,000 animals after full utilization day, and 2000 animals until then.
Resource1:TimePeriodStart2:FullUtilization	**2**	**21**	**DepopResource:** Day that all Resources are available. Up until this day, resources are available at 10% of full capacity.
Resource2:PerTimePeriod	**0.5**	**2**	**VaccinationResource:** a multiplier applied to the number of animals able to be vaccinated in a day. When multiplier = 1, the animals vaccinated per day (regardless of species) = 20,000 animals after full utilization

			day, and 2000 animals until then.
Resource2:TimePeriodStart2:FullUtilization	**2**	**21**	**VaccinationResource:** Day that all Resources are available. Up until this day, resources are available at 10% of full capacity.
Surveillance1:VisitFrequency:GenSurv	**3**	**10**	**GeneralSurveillance:** A probability distribution describing the number of time periods that will pass between visits to a farm following the first visit (described by the VisitDelay) prior to a farm being placed on the surveillance list. Poisson Distribution with means varied between low and high levels.
Surveillance1:DelayToDetection:GenSurv	**2**	**7**	**GeneralSurveillance:** A probability distribution returning the number of time periods from when the visit occurred to when that farm will receive the detected state (prior to a farm being placed on the surveillance list). Poisson Distribution with means varied between low and high levels.
Surveillance1:DetectionProbability[][][][]:GenSurv	**0**	**0.99**	**GeneralSurveillance:** A function describing the probability of an infected farm being detected at each visit by the number of time periods since the farm was infected. In our case, the function is constant, but would vary between the Lo and Hi values shown.

Surveillance1:DetectionProbability[][][sheep]:GenSurv	**0**	**0.95**	**GeneralSurveillance:** A function describing the probability of an infected **Sheep** farm being detected at each visit by the number of time periods since the farm was infected. In our case, the function is constant, but would vary between the Lo and Hi values shown.
Surveillance2:VisitDelay:GeneralAfterFirstDetection	**2**	**7**	**GeneralSurveillance_AfterDetect:** A probability distribution describing the number of time periods that will pass before a farm is visited after being placed on the surveillance list following a detected farm in the area. Poisson Distribution with means varied between low and high levels.
Surveillance2:VisitFrequency:GeneralAfterFirstDetection	**2**	**7**	**GeneralSurveillance_AfterDetect:** A probability distribution describing the number of time periods that will pass between visits to a farm following the first visit (described by the VisitDelay) while a farm is on the surveillance list. Poisson Distribution with means varied between low and high levels.
Surveillance3:VisitFrequency:GeneralSurv_Dairy_before	**0.5**	**3**	**GeneralSurv_Dairy_before:** A probability distribution describing the number of time periods that will pass between visits to a farm following the first visit (described by the VisitDelay) while a farm is on the surveillance list. Poisson Distribution with means varied between low and high levels.

Surveillance3:DelayToDetection:GeneralSurv_Dairy_before	**1**	**5**	**GeneralSurv_Dairy_before:** A probability distribution returning the number of time periods from when the visit occurred to when that farm will receive the detected state. Poisson Distribution with means varied between low and high levels.
Surveillance3:DetectionProbability[][][]:GeneralSurv_Dairy_before	**0.5**	**0.99**	**GeneralSurv_Dairy_before:** A function describing the probability of an infected farm being detected at each visit by the number of time periods since the farm was infected. In our case, the function is constant, but would vary between the Lo and Hi values shown.
Surveillance4:VisitDelay:GeneralSurv_Dairy_after	**0.5**	**2**	**GeneralSurv_Dairy_after:** A probability distribution describing the number of time periods that will pass before a farm is visited after being placed on the surveillance list following a detected farm in the area. Poisson Distribution with means varied between low and high levels.
Surveillance4:DelayToDetection:GeneralSurv_Dairy_after	**0.5**	**3**	**GeneralSurv_Dairy_after:** A probability distribution returning the number of time periods from when the visit occurred to when that farm will receive the detected state. Poisson Distribution with means varied between low and high levels.
Surveillance4:DetectionProbability[][][]:GeneralSurv_Dairy_after	**0.8**	**0.99**	**GeneralSurv_Dairy_after:** A function describing the probability of an infected farm being detected at each visit by the number of time

			periods since the farm was infected. In our case, the function is constant, but would vary between the Lo and Hi values shown.
Surveillance6:VisitDelay:SurvZone	**2**	**5**	**Surv_Zone:** A probability distribution describing the number of time periods that will pass before a farm is visited after being placed on the surveillance list following a detected farm in the area. Poisson Distribution with means varied between low and high levels.
Surveillance6:VisitFrequency:SurvZone	**2**	**7**	**Surv_Zone:** A probability distribution describing the number of time periods that will pass between visits to a farm following the first visit (described by the VisitDelay) while a farm is on the surveillance list. Poisson Distribution with means varied between low and high levels.
Surveillance6:DetectionProbability[][][sheep]:SurvZone	**0.7**	**0.95**	**Surv_Zone:** A function describing the probability of an infected **Sheep** farm being detected at each visit by the number of time periods since the farm was infected. In our case, the function is constant, but would vary between the Lo and Hi values shown.
Surveillance7:VisitDelay:Trace	**1**	**7**	**Surv_Trace:** A probability distribution describing the number of time periods that will pass before a farm is visited after being placed on the surveillance list following a detected farm in the area. Poisson Distribution with means varied

			between low and high levels.
Surveillance7:DelayToDetection:Trace	**1**	**5**	**Surv_Trace:** A probability distribution returning the number of time periods from when the visit occurred to when that farm will receive the detected state. Poisson Distribution with means varied between low and high levels.
Tracing1:ProbMovementForgotten[][]	**0.05**	**0.8**	**Tracing:** a probability that the infectious movement will be **forgotten** by the farmer and therefore never traced. Here, this is the same for all movement types.
Binary Variables			
Vaccination1:FarmClasses:DairyOnly	**0**	**1**	**Vacc_Zone:** Binary. If 0, then all cattle will be vaccinated. If 1, only Dairy premises, Dairy calf ranches, and feedlots will be vaccinated.
MovementRestriction3:ProbMovement Restricted:StopMarkets	**0**	**0.995**	**StopMarkets:** Binary variable defining the movement restrictions put on the market will be set for all markets (hi value) or only markets in a control area or surveillance zone.
COLOR CODE			
PARAMETERS FOR All FACTORS HIGHLIGHTED IN GREEN HAVE BEEN RETAINED FROM AXELSEN (2012)			
PARAMETERS FOR All FACTORS HIGHLIGHTED IN BLUE HAVE BEEN EITHER MODIFIED OR ADDED			

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